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LARYNGOSCOPE.

VOL. LXII APRIL, 1952. No. 4

FURTHER OBSERVATIONS CONCERNING THE TOXIC EFFECTS OF STREPTOMYCIN AND QUININE ON THE AUDITORY ORGAN OF GUINEA PIGS.*†

L. RUEDI, M.D.; W. FURRER, M.D.; F. LUTHY, M.D.;
G. NAGER, M.D., and B. TSCHIRREN, M.D.,
Zurich, Switzerland.

Two years ago we presented our first studies on guinea pigs treated with streptomycin. Testing the concha reflex (pinna reflex), we were able to prove slight losses of sound perception in the highest and lowest range of frequencies. Pronounced disorders of equilibrium were evident as well and have been filmed.

The histological examination of the animals' petrous bones showed normal structures in the cochlear and vestibular areas of the internal ear. On examining the serial sections of guinea pig brain, we found diminution of the number of ganglion cells and some glia nodules on the bottom of the fourth ventricle in the nucleus triangularis nervi VIII; we also observed slight changes, in form of plasma vacuolization, in the nucleus ventralis cochlearis and nuclear pycnosis within the ganglion cells. Shortly afterward, R. Caussé, for the first time, noticed histological changes in the peripheral vestibular apparatus of three mice poisoned with streptomycin, manifesting marked disturbance of equilibrium. His observations follow:

*This paper was read in French at the meeting of the Collegium Oto-Rhino-Laryngologicum in Rome, September, 1950.

†Clinic of Oto-Rhino-Laryngology at Zurich University and Physiological Institute at Berne University.

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"*a.* Disparition des cils des cellules sensorielles sur les cretes ampullaires et sur les macules autriculaires et sacculaires. Cette disparition était moins complète chez une souris dont les réactions vestibulaires n'étaient pas totalement supprimés au moment du sacrifice.

"*b.* Atrophie générale de l'épithélium des cinq terminaisons sensorielles vestibulaires, se traduisant par une moindre hauteur de cet épithélium, pouvant aller jusqu'à la moitié de celle d'ün organe normal. De meme les dimensions des cretes et des macules sont sensiblement réduites.

"Dans cette première série d'expériments l'organe de Corti ne parait pas intéressé par ce processus."

In additional investigations, Caussé confirmed his first finding of pathological changes within the peripheral vestibular apparatus. The loss of sensory hairs now appeared as a secondary process caused by preceding degeneration of the sensory cells of the cristae and maculae. In a second series of experiments on a mouse poisoned with streptomycin, Caussé found degenerative changes of the organ of Corti in the first cochlear turn. The absence of external and internal hair cells was accompanied by a degeneration of the corresponding nervous elements ascending to the ganglion spirale, which showed a decrease in the number of cells. Later, K. Berg found a similar pathological change in the peripheral auditory organ, in streptomycin-poisoned cats, which presented distinct disorders of equilibrium. In the cristae ampullares and the maculae utriculi and sacculi he observed degeneration of the sensory epithelium, narrowing of the epithelial layer due to the shrinking of cells and disappearance of the sensory hairs. The cat which had received the highest dose of streptomycin showed no traces of the organ of Corti in the lower and middle cochlear turns. On the same animal the author also observed impairment of hearing.*

After Caussé's first communication we reviewed our series of guinea pigs without being able to detect the loss of sensory hairs, which Caussé declared to be characteristic. In order to control the data reported by Caussé and Berg and presuming that our doses of streptomycin (usually 6 to 8 gm.) had been too weak to produce visible histological changes, we administered to another series of guinea pigs total quantities of 6 to

*Since then we have received the paper of Joseph E. Hawkins, Jr., on "Cochlear Signs of Streptomycin Intoxication." Hawkins shows a toxic action of streptomycin on the auditory system which occurs in the periphery at the end-organ, reducing primarily the aural microphonic response.

30 gm. of streptomycin per kg. of body weight. Aside from the effects of streptomycin on the vestibular apparatus, we were also interested in studying changes of sound perception due to streptomycin.

For the control of sound perception, during and after the treatment with streptomycin, we first determined the threshold of Preyer's pinna reflex for several test sounds. These were simultaneous to both ears. In the second place, we regularly made determinations on the right ear of the streptomycin-poisoned animal immediately before vivification. The values of the cochlear effect (Wever-Bray) were accomplished by means of the following experiment:

The cochlear potentials were always led off from the round window of the right ear, because this is the point of the strongest effect. A silver wire with ball point was used for this electrode. Silver chloride agar electrodes were used as indifferent electrodes by placing one on the throat and the other in the animal's anus. By means of a mercury switch each of the indifferent electrodes could be connected alternately with the amplifiers.

Leading off of the round window and the anus the ECG was produced simultaneously on the screen making it possible to count the pulse rate. Heart rate and form of the ECG provided indications for the depth of the anesthesia. The ECG disturbed the photographic registration of the cochlear potentials and the lead was changed to the throat electrode, for which the ECG was very small. Both electrodes were connected with a group of amplifiers, consisting of two-stage amplifiers in series. These were connected to an oscillograph and a loud speaker. Amplification obtained by this arrangement was about 60,000, i. m. volt corresponding to 24 mm. on the screen.

The cochlear potentialities were photographed as involution curves with slow speed of the time base and measured after calibration in microvolts. The lead was again connected with the anal electrode and the heart beats counted. They could be heard at the same time in the loudspeaker as beats of the ECG.

The frequencies of 2,000, 3,000, 4,000 up to 10,000 c.p.s. with sound intensities of 80, 90 and 100 db were used as stimuli. The sound was conducted directly to the guinea pig's ear without the use of a rubber tube. Less resonance phenomena were present in the sound field than with a rubber tube. On the other hand, care must be taken to avoid microphonic effects in the amplifiers.

The guinea pigs were anesthetized with urethane (1 gm. per kg. of body weight, 10 per cent solution, intraperitoneal administration). Good oxygen supply is important. From the moment of injection until the beginning of the operation, the animals were placed under a glass bell aired with oxygen. As soon as the narcosis was deep enough (generally after 20 minutes), tracheotomy was performed and oxygen administered through the tracheal tube.

The round window was exposed and the animal immobilized by means of a stand and a head holder. In order to eliminate every muscular action the animal was then paralyzed with curare (0.3 mg. of tubarine). Artificial respiration was maintained by a respiration pump with oxycarbon. This type of narcosis maintains the circulation in a fairly good condition. In our experience it was found of great importance for the maintenance of the cochlear potential.

The whole preparation was kept within a Faraday cage, shielding it from external electrical disturbances.

For histological examination we finally prepared the petrous bones and the brain of the vivifixed animals, sectioned in series and stained.

I — Experiments with Streptomycin.

Nine guinea pigs were lost in the experiments, five animals gave results which were completely investigated. Fig. 1 represents body weight, quantities of streptomycin administered, duration of treatment, the results of the equilibrium and sound perception tests.

Streptomycin - Intoxikation

Nr	Gewicht g	Einzel-Dosis g	Tage	Gesamt Dosis g	g/kg	Kst.-Reakt.	Pinna-Reflex	Cochlea-Effekt
1298	480	0,05 0,02 0,05	33	6,59	13,7	path	0	0
1414	700	0,02 0,05 0,05	98	13,85	19,8	path	0	0
1459	550	0,05 0,05 0,05 0,1 0,12 0,15	160	14,61	26,7	path	stark abgeschwächt	abgeschwächt
1416	600	0,05 0,05 0,05 0,1	134	21,37	35,5	path	stark abgeschwächt	abgeschwächt
1409	550	0,05 0,05 0,05 0,1 0,12 0,15	160	30,69	55,8	path	stark abgeschwächt	abgeschwächt

Fig. 1. Streptomycin intoxication of the guinea pig.

All the guinea pigs showed more or less clearly the typical phenomena of irritation and deficiency of the vestibular apparatus. In previous experiments we were able to demonstrate

these in a film; furthermore, during the administration of streptomycin, all animals showed a loss of sound perception of a very variable extent.

The *histological examination* of the petrous bones regularly showed changes of the sensory terminals within the peripheral vestibular apparatus, though variable with respect to their extent. These were similar to those first described by R. Caussé for the ears of mice, and afterward by K. Berg for the ears of cats. In guinea pigs we found the following:

1. The cristae (see Fig. 2) and maculae (see Fig. 3) displayed a clear reduction of sensory epithelium. This formed

Fig. 2. Crista ampullaris posterior degenerated after protracted injection of streptomycin (Animal No. 1416).

an area in which numerous dark and nearly round nuclei were recognizable. They were without cellular outlines and often without cuticular border. The injury started in the sensory cells, which gradually disappeared, while the supporting cells became swollen, and perhaps even multiplied, as described by Caussé. Generally, the cristae ampullares and the maculae utriculi showed more changes than the maculae sacculi.

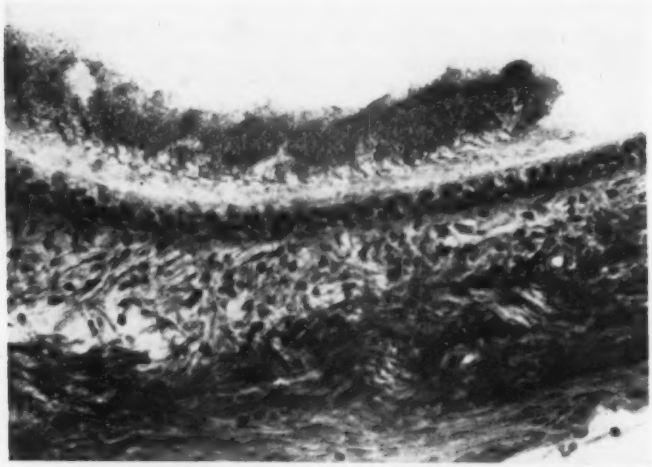

Fig. 3. Marked degeneration of macula utriculi after protracted injection of streptomycin (Animal No. 1298).

2. The degeneration of sensory cells was accompanied by the loss of sensory hairs, which at first could be observed separately and later as an expanding surface.

3. In the most peripheral fibres of the nervus vestibularis the injured cristae ampullares displayed an ascending degeneration in the form of medullary loss. The nerve pathways in the stroma of the cristae and in the perforating bony channels could be followed only by means of Schwann's sheaths, which seemed to be empty. The changes in the nervous apparatus spread to the ganglion vestibulare (see Fig. 4), which was also clearly damaged; some of its ganglion

cells were pale shadows, others distinctly shrunken, so that the nucleus could not be distinguished from protoplasm. The capsular cells of the degenerating ganglion cells were obviously increased. The nerve fibres arising from the ganglion vestibulare and ascending to the center were of normal appearance.

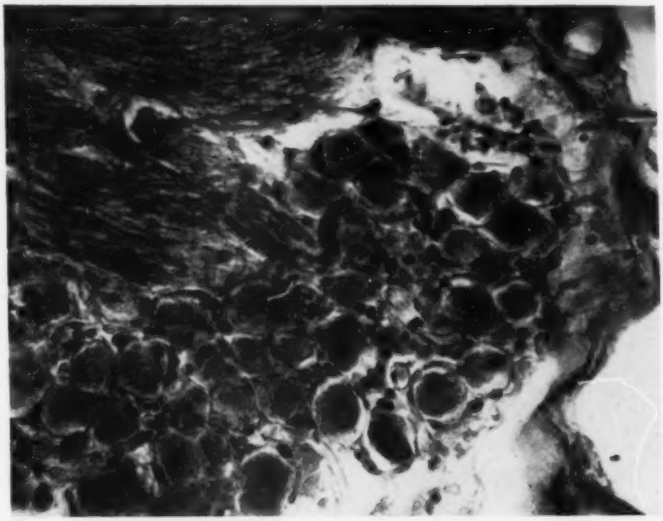

Fig. 4. Ganglion vestibulare with signs of degeneration after protracted injection of streptomycin (Animal No. 1298).

In the *cochlea* of all streptomycin-injured guinea pigs more or less marked pathological changes occurred, particularly in the organ of Corti. These correspond fundamentally to the findings of R. Caussé (in mice) and K. Berg (in cats). Guinea pig No. 1298 exhibited severe organic lesions. It lost the pinna reflex under streptomycin treatment and no cochlear effect could be demonstrated. The organ of Corti (see Fig. 5) disappeared symmetrically on either side in the entire area of the first turn.

The vestibular surface of the basilar membrane was covered by a low cuboidal epithelial layer with some cellular detritus (see Fig. 6). In the sulcus spiralis internus the cell layer was lacking, the tip of the tectorial

membrane was surrounded by a homogeneous mass with inclusions of cellular detritus. In the sulcus spiralis externus Claudius' cells have disappeared, as well as the epithelium from the stria vascularis which normally covers the eminentia spiralis. Following the lesions of the organ of Corti from their starting point at the windows through the cochlea,

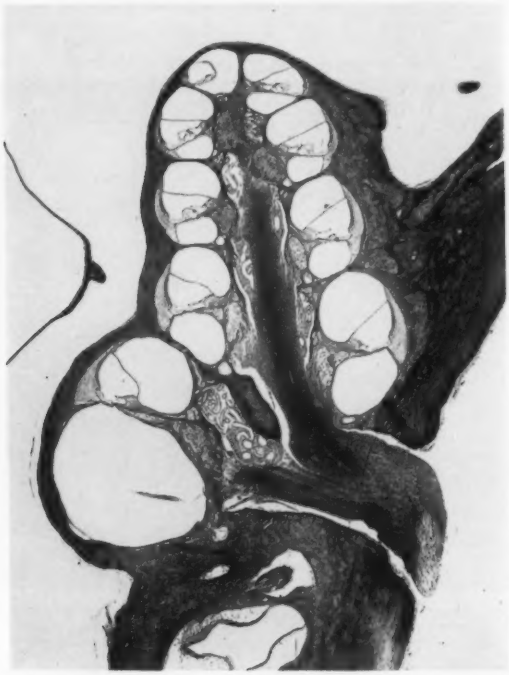

Fig. 5. Longitudinal section of the cochlea showing degeneration of the organ of Corti in the first and second turn, due to protracted injection of streptomycin (Animal No. 1414).

the vault of the papilla spiralis with the outer pillars of Corti's rod cells and the most lateral cells of Deiter's, relatively Hensen's, reappear again from the first turn onward. In the interspace there is a cavity roofed by the lamina reticularis and formed by the junction of Nuel's space and the outer tunnel and by the degeneration of hair cells and supporting cells. Ascending a bit further in the cochlea, the inner rod cell is flanked again by an internal hair cell. At the end of the second turn, we arrive at the borders of the injured area where the transition to the normal histological status of the organ of Corti rapidly proceeds with the reappearance, first, of Deiter's cells; then, of the two external hair cells (situated on the outer aspect) and, finally, the medial external hair cell, with its nucleus and boundaries

(*cp.*, the corresponding findings in noise and report traumata: "Acoustic Trauma," by L. Rüedi and W. Furrer). In the area where the organ of Corti has suffered the severest lesions the mesothelial cells of the basilar membrane are equally degenerated and adhere to the membrane in irregular order. Some of these cell bodies are flattened and some of the nuclei are shrunken. Wherever the organ of Corti has disappeared an ascending degeneration of the afferent nerve fibres of the ganglion spirale can regularly be demonstrated with changes in the ganglion spirale and further degeneration of the fibres leading to the VIIIth cranial nerve.

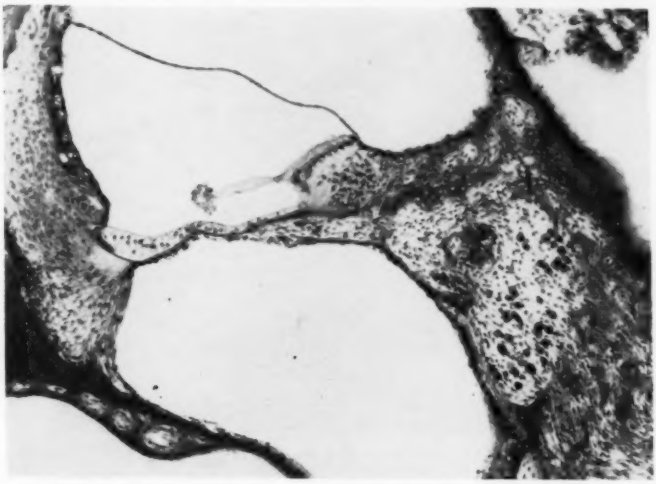

Fig. 6. Area from Fig. 5, large magnification. Absence of the organ of Corti in the first turn and ascending degeneration of the corresponding nervous apparatus.

Instead of a densely braided bundle of nerve fibres there are loose braids of varicose nerves in the bony channels of the modiolus. For long stretches they are without medulla and only recognizable by means of Schwann's sheaths. Between the degenerated nerve fibre cells containing fat and pigment, granules have engulfed the products of tissue destruction. In the corresponding ganglion spirale (cochleare) the number of ganglion cells has greatly decreased. The remaining cells are shrunken, their outlines are irregular and it is difficult to distinguish the dark nuclei from the cytoplasm. The ascending nervous degeneration can clearly be followed over the ganglion spirale and into the nerve fibres which lead to the trunk of the VIIIth cranial nerve.

In the area where the organ of Corti disappeared as in the entire first turn, the *stria vascularis* also exhibited marked pathological changes. The normal threefold stratification of the epithelial nuclei was disturbed (see Fig. 7): the single nuclear layer near the surface cannot be distinguished without difficulty from the palisade-like grouped nuclei of the middle cylindrical cells which are not easily differentiated from the next

adjacent stroma. The number of cylindrical epithelial cells appear decreased. Most of the stria vessels are wider than normal and the stria epithelium on the whole is clearly narrowed. Some points give the impression that the superficial cellular debris is being resorbed through the delicate walls of the wide capillaries.

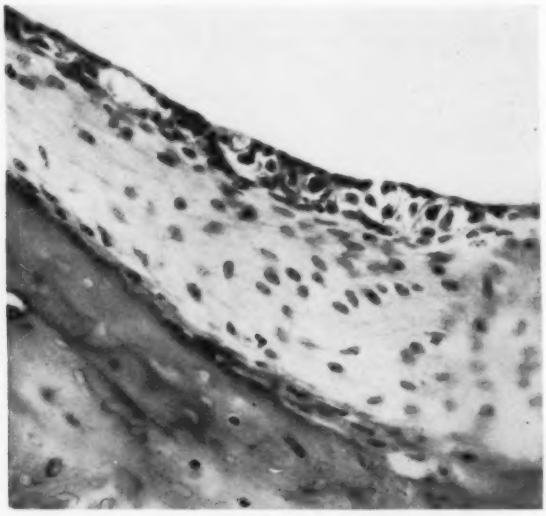

Fig. 7. Degeneration of stria vascularis in the first turn after protracted injection of streptomycin (Animal No. 1298).

As in the study of acoustic trauma, the functional and histological results of our streptomycin experiments on the cochlear apparatus have been represented in a diagram, in the first half of which we indicate the quantity of administered substance, the time of the treatment and the results of the sound perception tests expressed as diminution of the pinna reflex (in decibels). The latter are compared to the status quo and below to the loss of potential (measured in microvolt) observed in the cochlear effect as referred to normal average values. The second half of the table represents systematically the histological alterations of the cochlear area. The four vertical divisions correspond to the four turns of the guinea pig's cochlea. The horizontal divisions show the portions which are specially vulnerable: the stria vascularis,

the mesothelial cells, the external hair cells, the internal hair cells and the adjacent ganglion spirale. By means of serial sections, the histological changes of these different areas can be localized to some degree within the four cochlear turns so that it is possible to record them in form of black faces or hatchings on the corresponding portions of the graph.

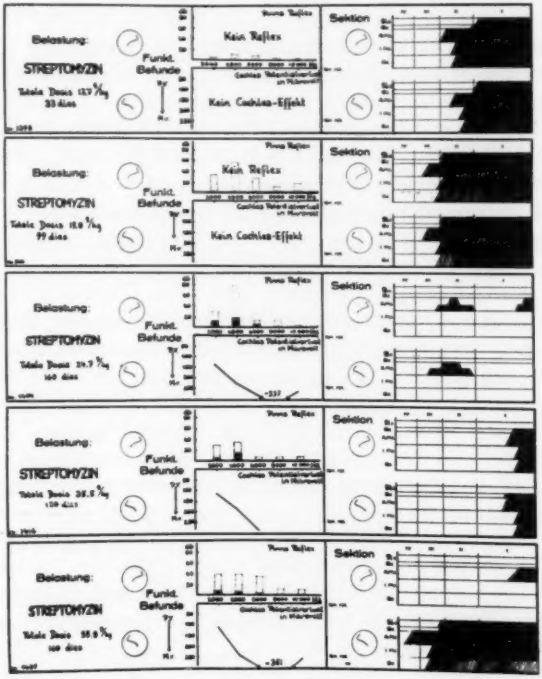

Fig. 8. Schematic digest of the functional and histological results obtained by protracted injection of streptomycin.

By joining the diagrams of five streptomycin-poisoned guinea pigs, we have the possibility of comparing synoptically the quantity of substance administered, the functional loss and the organic lesion. The following details seem worth mentioning.

a. Both methods for measuring the sound perception give quite concordant results; it, therefore, seems that the pinna reflex test as well as the cochlear effect are suitable as functional tests of the guinea pig's ear.

b. The loss of sound perception for streptomycin-treated animals was not in proportion to the quantity of drug administered per kilogram of weight.

Animal No. 1298 received, during 33 days, 13.7 gm./kg. with disappearance of the pinna reflex for all test sounds and the cochlear effect was no longer measurable. To all appearances this animal became deaf due to the administration of streptomycin. On the other hand, Animal No. 1416, after 128 days' administration and a total quantity of 35.5 gm./kg., showed only a strong damping of the pinna reflex and the cochlear effect; therefore, we found that certain guinea pigs are much more sensitive to streptomycin than others.

c. Considering the black zones of injury in the diagrams, nearly all cases show symmetrical damage to both auditory organs. Animal No. 1409, which received the largest dose (55.8 gm./kg.) exhibited a very slight histological damage of the right ear (disappearance of the external hair cells in the beginning of the first turn). The left ear experienced a most severe degeneration with complete loss of the organ of Corti up to the third turn.

d. Comparing the functional losses with the histological changes, it seems that the entire loss of sound perception is regularly accompanied by a complete disappearance of the organ of Corti within the first turn. The animals with minor functional damage exhibited histological changes of lesser degree, such as circumscribed loss of the external hair cells (Animal No. 1484) or complete loss of the organ of Corti in only the beginning of the first turn (Animal No. 1416); consequently, for this animal the sound perception test was negative above 6,000 c.p.s. The guinea pig with different lesions of either ear still hears to some extent with the right ear, for which the cochlear effect was tested.

e. Histological damage first became visible in the external hair cells. As soon as the internal hair cell was equally damaged, which means the beginning of disappearance of the organ of Corti, pathological changes could also be found in the corresponding cochlear area of the stria vascularis.

The histological examination of the *central nervous system* of streptomycin-injured guinea pigs shows again, as in our former findings, certain pathological changes. These are in form of isolated glia nodules and some degeneration of the ganglion cells, located in the area of the vestibular nuclei on the bottom of the fourth ventricle and in the nucleus ventralis cochlearis; nevertheless, there is no proportion between the extent of these minor pathological signs and the functional loss. We do not consider these nuclear changes as specific for streptomycin injury.

Simultaneously with the streptomycin tests, two other groups of guinea pigs received daily small quantities of *hydrochloric quinine* and *sodium salicylate*, following the same order of experimentation. Since the salicylate experiments have not yielded any results so far, we report our observations on quinine-poisoned guinea pigs.

It has been known for quite a long time that quinine produces hearing impairment, but the point of noxious attack in the aural region has not been definitely determined. According to Kirchner and Mosher, quinine gives rise to vascular contusion and hemorrhage in the cochlea. According to Orembowsky and Wittmaack, the drug attacks the peripheral nervous apparatus, while Schröder and Hinsberg, as well as Pellegrini and Nathan, reported changes of the ganglion cells in the central nervous apparatus, caused by quinine. Covell suggested that changes of pressure in the ductus cochlearis and impairment of the oxygen supply were caused by the action of quinine; moreover, he assumed a direct toxic effect of quinine on cell protoplasm, *producing degeneration* of the stria vascularis and the external hair cells. It is rather astonishing that in previous *in vivo* experiments so

little attention was given the relation between degree and form of functional loss on one hand and the extent and localization of the histological changes on the other.

II — Quinine Experiments.

Having lost 23 guinea pigs, five animals were thoroughly investigated. The best method of quinine administration seems to be the introduction of the drug into the throat by means of a short, wide glass tube. Even this careful form of application causes death to a considerable number of guinea pigs, which die spontaneously during the treatment, obviously poisoned.

Fig. 9 shows the weight of the animals, the single and total doses administered per kilogram of body weight, the results of the equilibrium and sound perception tests. The latter was regularly performed by examination of the pinna reflex and of the cochlear effect. Under protracted administration of quinine to guinea pigs, we found no pathological changes of the vestibular function, but the hearing tests showed a significant and even complete loss of sound perception in all animals.

Chinin — Intoxikation

Nr	Gewicht g	Einzel-Dosis g	Tage	Gesamt-Dosis g	g/kg	Vest.-Reakt.	Pinna-Reflex	Cochlea-Effekt
1458	800	0,1	95	7,7	9,6	—	0	0
862	600	0,1	248	14	23,3	normal	0	0
1272	400	0,05 0,1	182	9,8	24,5	—	0	stark abgeschwächt
875	650	0,1 0,2 0,1	390	32	49,3	normal	stark abgeschwächt	abgeschwächt
828	250	0,05 0,1 0,2 0,1	522	28	112	normal	stark abgeschwächt	abgeschwächt

Fig. 9. Quinine intoxication of the guinea pig.

The *histological investigation* of the petrous bones of the five guinea pigs presented normal conditions in the peripheral sensory terminals of the *vestibular apparatus*. On the other hand, the *cochlea* of quinine-poisoned guinea pigs regularly exhibited more or less marked changes of the organ of Corti and the corresponding nervous apparatus and stria vascularis. In Animal No. 1458, the vertical cochlear section displays degeneration of the organ of Corti in the lowest half of the

Fig. 10. Longitudinal section of the cochlea showing degeneration of the organ of Corti in the beginning of the first turn, due to protracted administration of quinine (Animal No. 1458).

first turn. By high magnification of the area we observe the loss of the external hair cells and decomposition within the internal hair cells and the supporting elements. Animal No. 862 showed more injurious effects. In the first turn the organ of Corti has completely disappeared, only a narrow epithelial border remaining on the basilar membrane.

Wherever the organ of Corti is lacking, the corresponding *nervous apparatus* shows an ascending degeneration with medullary loss in the afferent and efferent fibres of the ganglion spirale where the number of cells has strongly decreased.

In the area of the main damage the *stria vascularis* (see Fig. 11) is regularly injured by a decrease in the central layer of cylindrical cells and by formation of cysts.

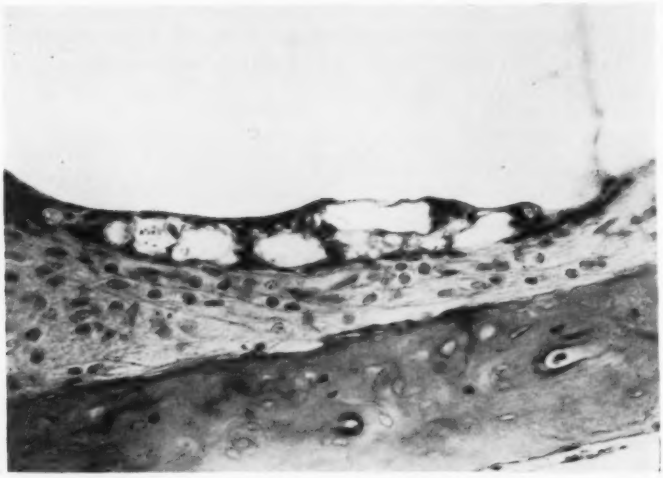

Fig. 11. Cystic degeneration of stria vascularis in the first turn following protracted administration of quinine (Animal No. 1272).

The diagrams of the five cases of quinine damage show the quantity and administration period of the drug and the functional loss and the corresponding histological changes within the cochlear area. The detailed observation of functional disorders and histological defects gives the following results:

a. The quinine tests confirm the agreement of two different methods concerning the results of sound perception, as already observed in the streptomycin experiments.

b. Certain guinea pigs are much more sensitive to hydrochloric quinine than other animals. No. 1458, *e.g.*, is completely deaf after 95 days' administration of 9.6 gm./kg. No. 828, however, having received 112 gm./kg. within 522 days, shows only a diminished pinna reflex and the cochlear effect.

c. The injured zones, in black on the cochlear scheme, are distributed with remarkable symmetry in the hearing organs of each animal.

d. When the functional losses are compared with the histological changes the complete lack of sound perception is again accompanied by the regular and entire absence of the organ

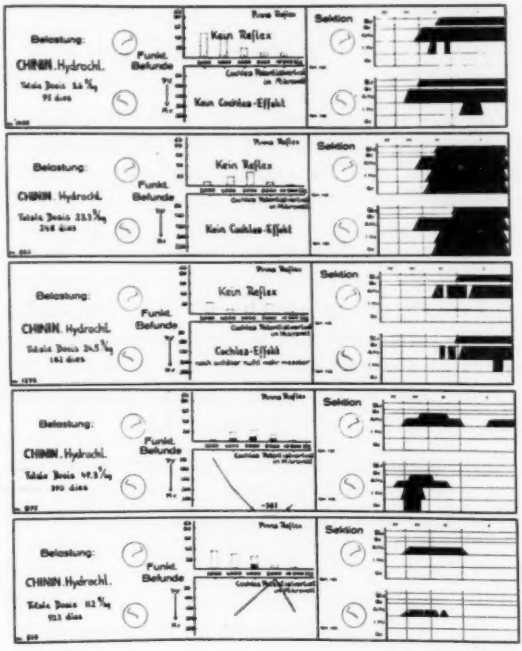

Fig. 12. Schematic digest of the functional and histological results obtained by protracted administration of quinine.

of Corti in the entire first turn. The animals with minor functional damage present circumscribed losses of the external hair cells only in the higher turns.

e. Quinine injury first appears histologically in the external hair cells, thus corroborating the findings published by

Covell. If the remaining portions of the organ of Corti are also affected, the corresponding stria vascularis presents pathological changes.

The histological investigation of the *central nervous system* of quinine-injured guinea pigs does not reveal pathological changes on the bottom of the fourth ventricle in the area of the vestibular and cochlear nuclei.

SUMMARY.

The protracted injection of large doses of streptomycin to guinea pigs produces marked functional damage of the equilibrium apparatus and a loss of sound perception. It is true that here and there in the nuclear area of the acoustic nerve previously described changes are present. They do not seem to be a specific tissue alteration due to streptomycin. According to our findings, the vestibular and cochlear functional losses are mainly correlated with the degeneration in the sensory terminals of the peripheral vestibular apparatus, as pointed out by R. Caussé and K. Berg; moreover, the severest degeneration of the organ of Corti and of the corresponding nervous apparatus, as well as pathological changes of the stria vascularis, are found in the lowest cochlear turns.

The protracted administration of large doses of hydrochloric quinine provokes marked loss of sound perception. This functional damage is histologically correlated with degeneration of the organ of Corti and the corresponding nervous apparatus. It extends over several turns and is combined with pathological changes of the stria vascularis. The degenerative processes caused by quinine begin in the external hair cells, as shown by Covell.

We regret that Raoul Caussé did not live to enjoy this confirmation of his investigations on experimental streptomycin lesions of the ear.

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RESUSCITATION OF THE HEART IN THE PRACTICE OF OTOLARYNGOLOGY.*

MERRILL LINEBACK, M.D.,
Boston, Mass.

Of the emergencies that may and occasionally do occur in the operating room perhaps the most urgent is "cardiac arrest." Its onset is sudden and unexpected in patients who have been examined preoperatively and found to have normal hearts and lungs. The speed with which diagnosis and treatment is made determines whether the patient will recover either wholly or in part, or die of cardiac asystole. An adequate supply of oxygen to the brain by rapid restoration of the heart's pumping action is of prime importance: delay beyond three and one-half or four minutes means varying degrees of cerebral damage and if longer than four to five minutes probably failure to resuscitate the patient.[1]

"Cardiac arrest" is cessation of the pumping action of the heart due either to cardiac standstill or to ventricular fibrillation. It is most likely to occur under the following conditions:

1. During rapid induction of anesthesia.
2. During endotracheal intubation or extubation.
3. During manipulations in the neck, notably in region of the carotid sinus,
4. Toward the end of long and difficult procedures, particularly intrathoracic operations,
5. Sudden change of position of patient, particularly at the end of lengthy procedures.

Because of the circumstances of the asystole during induction with a general anesthetic prior to endoscopy for removal

*From the Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Boston, Mass.

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of a large foreign body in the upper end of the esophagus and the patient's practically complete recovery, it is felt that the following case should be recorded:

Mrs. J. A. M., age 67 years, was admitted to the Massachusetts Eye and Ear Infirmary for the first time on June 2, 1951, with the complaint of pain in the throat and a "choking sensation" of six hours' duration following ingestion of a piece of Washington pie "that was not homemade." She had dysphagia but no cough, hoarseness or hemoptysis. Prior to admission her throat pain became less. Further history obtained from her sons revealed that prior to eating the pie she had attempted eating a piece of breast of chicken. They reported that since early morning she had seemed bewildered and confused, though they attributed these portents to her age.

Past history revealed that 25 years ago she had cholecystectomy and six weeks later, laparotomy for bleeding peptic ulcer. Ten years ago she had a transient episode of "heart stopping" late at night, which was relieved by her husband pounding on her chest. No physician examined her at the time. One year ago, while on a motor trip through Virginia during the Summer, she sustained a fractured skull, lacerations of her forehead, and a fractured left tibia in an accident. Two months later, just out of her casts, while watching television she arose to turn the set off and fell, sustaining a fracture of her right hip. During hospitalization for this second fracture she had what her physicians described as a "heart attack" in spite of normal EKG's. Since healing of the hip fractures she had been carrying on her routine housekeeping duties without complaint.

General physical examination revealed her blood pressure to be 150/90, no enlargement of the heart, lung fields clear, no edema of the extremities and no dyspnea. Local examination revealed pooling of saliva in the pyriform sinuses and tenderness in the lower neck to deep palpation on either side.

Laboratory examination revealed no albumin in the urine, but a trace of sugar was present. The fasting blood sugar was 83 mgm. per cent and blood NPN was 27 mgm. per cent. Urinalyses were repeated several times during her hospital stay and were negative for sugar each time. At fluoroscopy the day following admission a barium swallow revealed a large nonopaque foreign body in the upper end of the esophagus. Complete blood count revealed white cells, 7,300; red cells, 4.24 million; a hemoglobin of 13.8 gm. per cent and a differential showing polys, 70; lymphs, 23; monos, 5, and eos, 2 per cent. Her blood type was group A, Rh positive.

The day following admission she was premedicated with 60 mgm. of luminal intramuscularly and 0.4 mgm. of atropine s.c. at 11 A.M. and sent to the O.R. for general anesthesia and esophagoscopy 45 minutes later. She appeared composed and unconcerned about her forthcoming ordeal. The nurse anesthetist reported that induction was quiet, but about 12 to 13 minutes after starting, the patient suddenly went limp with complete relaxation and no pulse, heart beat or respiration could be detected. The Roentgenologist bringing the lateral neck films fortunately was passing the anesthesia room and, seeing the anesthetist's predicament, summoned the resident and together they attempted the following emergency measures while an endotracheal tube carrying oxygen was being inserted by the anesthetist: manual compression of the chest in artificial respiration was tried and when this failed, forceful thumping of the precordial area

with the closed fist. Both procedures were to no avail, and when the Roentgenologist suggested anal dilatation, the resident was called to the head of the patient to check the position of the endotracheal tube. He found this to be in the trachea and the vocal cords in the cadaveric position. The patient meanwhile was showing a mottled cyanosis and at this point the single remaining method of resuscitation was cardiac massage. While the resident hurried to an adjacent room for a knife, the chief anesthetist for the infirmary arrived and together all concerned quickly wheeled the patient into a vacant O.R., where artificial respiration with 100 per cent oxygen through a CO_2 absorption anesthesia apparatus was immediately instituted and the patient was placed in Trendelenburg position. At the suggestion of the chief anesthetist thoracotomy was performed rather than the transabdominal approach originally decided upon by the resident. Without preparing the skin, an incision was made on the left, beginning at the sternal margin and carried out to the anterior axillary fold below the nipple and down to the fifth intercostal space. The next stroke cut the intercostal muscles and opened the pericardial sac. No bleeding was encountered. Into the pericardial opening two fingers could be inserted and the heart was found to be still and in systolic contraction. Massage was begun by pressing the heart rhythmically once a second against the sternum from the base to the apex and within 30 seconds beating resumed and continued of its own accord. An assistant then began an I.V. infusion of saline and dextrose. Artificial respiration being maintained meanwhile, with resumption of the heart beat several bleeding points were located and tied and the patient's color returned to pink. She began shortly to respond to painful stimuli such as suturing the chest wall, which was closed tight in layers without drainage and a pressure dressing was applied.

At this point it was decided, rather than to leave the foreign body in place and go down with the esophagoscope at a later date, running the risk of recurring cardiac arrest, that removal of the body be done immediately even though the patient was only lightly anesthetized. Being alive, however, there was a possibility that she had been anoxic enough to depress the sensorium, and in that event anesthesia would be useless. About half an hour after cardiac massage the Mosher full-lumen esophagoscope was passed without difficulty, but due to the large size of the body and the friable meat attached to what was apparently cartilage, it was impossible to remove it. Spasm of the cricopharyngeal pinchcock because of the light anesthesia also helped to prevent removal of the foreign body. As a consequence this was pushed into the stomach and No. 20 and No. 24 esophageal bougies were passed easily through the lower end of the esophagus into the stomach. Careful inspection of the mucosa as the Mosher esophagoscope was withdrawn revealed no lacerations. An EKG taken while the patient was still on the table revealed standard and unipolar leads were normal.

Pulse on resumption of cardiac activity was 132 per minute, blood pressure was 106/70; at the end of both procedures pulse was 110 and pressure 108/80. Neosynephrine 3 mgm. I.M. and 0.5 mgm. I.V. 20 minutes after starting the heart was given because the pressure was falling to 80/60. Consciousness was not regained for about 36 hours, during which time she was a "vegetable."

Postoperatively she was given I.M. quinidine lactate 0.15 gm. every eight hours for six times. Crysticillin 300,000 units and streptomycin 0.5 gm. I.M. were given twice daily as a prophylactic against pulmonary infection. Beginning about 36 hours postoperatively she slowly regained awareness of objects and persons around her. Memory for recent events

was gone, but she could recall details of her "heart attack" one year ago, such as "pain and numbness of both arms." During the ensuing week her memory had returned for all things up to the day of swallowing the foreign body. By the end of the week she was vague about the first two or three postoperative days also; but continued to improve steadily. On the third day after operation she had a typical anginal attack, which was relieved with 0.3 mgm. nitroglycerine sublingually. A portable chest film showed slight amount of fluid in the left pleural space but no displacement of the left lung root, no mediastinal shift, and no pericardial effusion. Repeat EKG's showed "serial improvement in T waves of the limb leads," and chest films revealed no increase in fluid in the left base. She was out of bed on the fifth postoperative day and continued up at increasing intervals, being discharged well on her twelfth hospital day. At her last OPD visit for checkup she was well and happy in her usual housekeeping activities.

DISCUSSION.

Otolaryngologists as specialists in head and neck surgery should be aware of and familiar with the treatment of a surgical emergency that may occur once during a lifetime of practice. Unless cardiac arrest is handled properly the results may be disastrous. One must have on hand a plan of action with the necessary tools readily available.[2]

In thinking of cardiac resuscitation, death from the usual medical causes is not included.[3] Success is seldom to be expected unless the arrest occurs in the operating room. Even then success is unlikely when dealing with a patient with severe myocardial injury. A favorable case is one having an overdose of anesthetic or is sensitive to either the local or general anesthetic. The calamity occurs most often during light anesthesia in either the induction phase or recovery when the myocardium is known to be more irritable than normal.[4] Delay in the diagnosis of cardiac arrest is the chief factor in failure.

Thoracotomy is considered to be a diagnostic measure, particularly when an EKG machine is not available routinely or immediately and when the heart is not exposed as it is in chest operations. The immediate restoration of the circulation and with it oxygenated blood to the brain in three to four minutes is the single most essential therapeutic measure.

In those hearts with no demonstrable lesion, anoxia or overdose of anesthetic is not apparently contributory to the onset of cardiac arrest and Johnson and Kirby think possibly that

a vagovagal reflex phenomenon is responsible. In the case presented with this paper the possibility of such a reflex being present must be considered. In the upper end of the esophagus there was an unusually large foreign body present during induction of anesthesia. This could conceivably set up vagovagal reflexes especially during light anesthesia, with the patient trying either to swallow or to expel it; however, the preoperative status of the patient's heart is not known, though presumably it was within normal limits; blood pressure was 150/90 and the chest was "clear to auscultation and percussion." What effect her "heart attack" a year ago had on her arrest is also a matter for conjecture. The EKG taken after massage while she was still on the table was within normal limits, so presumably her preoperative cardiac activity was normal. The more likely cause in the present case was probably what to this patient was a relative overdose of anesthetic as it occurred within 12 minutes after anesthesia was started, especially since the anesthetist reported the induction as proceeding smoothly.

As will be seen from the case record, close teamwork between the surgeon and anesthetist is essential to success. In fact it is desirable for the anesthetist to direct the procedures necessary for resuscitation as he has minute to minute control over the patient from the very outset. The following steps should be carried out in the order given:

1. Presumptive diagnosis of cardiac arrest should be made when a sudden failure of blood pressure and pulse occurs, often called attention to by sudden failure of respiration, especially when accompanied by lack of capillary filling after blanching, and presence of mottled cyanosis.

2. The anesthetist must immediately inform the surgeon, who should then take appropriate steps to confirm the diagnosis and initiate treatment. Without delay the surgeon should undertake to restore the pumping action of the heart:

a. if the thorax or abdomen is not already open, he should perform an immediate left thoracotomy through the fourth or fifth interspace, taking care

to avoid the internal mammary artery which lies quite constantly within 1 cm. lateral to the sternal cartilage. He should then deliberately squeeze the heart at approximately 60 times per minute in such a way as to empty the heart.

b. if the abdomen is open, the surgeon extends the incision so that he may massage the heart through the dome of the left diaphragm. If the circulation is not sufficient the diaphragm may be opened anteroposteriorly in its central tendinous portion and the hand inserted directly into the pericardial cavity, grasping the ventricle in the palm of the hand. If massage is effective a peripheral pulse is obtained.

3. Artificial respiration at a normal rate with 100 per cent oxygen is best carried out by bag compression of a CO_2 absorption anesthesia apparatus. Endotracheal intubation will usually facilitate artificial respiration. If cardiac arrest occurs during intubation, of course, the tube should be withdrawn; if during extubation or before intubation, it should be replaced.

4. To provide a route of further medication an intravenous infusion of an isotonic solution, saline or glucose, is started by an assistant as soon as possible. If a blood transfusion is indicated the intra-arterial route should be considered. Decision as to the nature of the cardiac disability, standstill or ventricular fibrillation, is made by direct inspection of the heart or by EKG.

5. If the diagnosis is cardiac standstill: give 0.2 to 0.3 cc. of a 1:1,000 epinephrine[5] diluted 10 times with normal saline; that is, 2 to 3 cc. of 1:10,000 epinephrine into the right auricle. This solution may be injected into the jugular vein if the heart is not exposed, cardiac massage and artificial respiration continuing meanwhile.

6. If the diagnosis is ventricular fibrillation, it can be corrected by electrical stimulation[6] or, it is said, by the I. V. or intracardiac injection of 3 to 10 cc. or 1 per cent procaine

HCl. There is, however, no conclusive evidence to support this.[7] The dose may be repeated but it must be remembered that procaine is a profound cardiac poison.

SUMMARY.

A successful case of cardiac resuscitation following cardiac standstill is reported and discussed. Every otolaryngologist should be familiar with the procedure in diagnosis and handling of these cases and should have in mind a plan of action to be instituted when confronted with such an event. Close cooperation between the surgeon and anesthetist is emphasized. Immediate restoration of the blood oxygen to the brain within three and not more than four minutes is mandatory if resuscitation is to be successful and the psyche of the patient is to be preserved. The simplest route to the heart for the otolaryngologist or other surgeon is the most direct one; that is, through the anterior chest wall in the left fourth or fifth intercostal space, providing the chest is not already open. The value of thoracotomy as a diagnostic procedure in cases of suspected cardiac arrest is stressed. It is no more harmful to the patient and is often lifesaving.

Acknowledgment is made to Dr. John Bunker, of the Anesthesia Department of the Massachusetts General Hospital, who at the time was the chief anesthetist at the Massachusetts Eye and Ear Infirmary, for his help in preparing this paper, particularly the outline of management.

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243 Charles Street.

THE CARDIOESOPHAGEAL JUNCTION— A HISTOLOGIC STUDY.*†

GERHARD D. STRAUSS, M.D.,
Milwaukee, Wis.,
and
JOSEPH M. LUBITZ, M.D. (by invitation),
Wood, Wis.

Recent advances in medicine have made possible the relatively safe surgical attack on lesions of the esophagus. Advances in therapy have focused increasing attention upon areas which hitherto have been mainly of diagnostic importance, or at best a field for primarily endoscopic or for palliative measures. The cardioesophageal junction is an area which has fascinated otolaryngologists for several generations. Lately, however, considerable interest has been aroused in the etiology of inflammatory and ulcerative lesions of the esophagus, along with such conditions as benign stricture, short esophagus and cardiospasm. The increasing frequency of resection of the esophagus for carcinoma has created wide interest in the study and classification of neoplasms of this area.

We, therefore, felt that it would be worthwhile to go back to a study of the normal histology of the lower esophagus in order to understand better the pathologic aberrations. Our interest was mainly directed to the glandular elements, which seemed to hold the key to many problems of clinical interest. The literature in regard to these structures was reviewed and information was found to be remarkably scarce and to some extent controversial. For example, variations of opinion on whether islands of gastric mucosa can be found in the esopha-

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†From Departments of Otolaryngology and Pathology, Marquette University School of Medicine, and U. S. Veterans' Hospital, Wood, Wis.

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gus were encountered. Maximow and Bloom[1] state that the number and development of the cardiac glands, as well as of the islands of the gastric mucosa in the esophagus, are subject to great individual variations. According to some investigators, they state that the presence of this ectopic epithelium may be of some importance for the origin of diverticula, cysts, ulcers and carcinoma of the esophagus. On the other hand, "Jordan's Textbook of Histology"[2] makes no mention of such ectopic stomach mucosa.

Feldman and Zinn[3] state that gastric heterotopia is not rare and that ordinarily the secretion from this is neutralized by saliva. They believe that it is possible with extensive heterotopia, accompanied by spasm of the cardia, to accumulate considerable quantities of acid in the esophagus; however, Ireland[4] in a comprehensive study of over 100 autopsy specimens at Massachusetts Eye and Ear Infirmary states that he does not believe that true gastric mucosa is ever present in the esophagus. He believes that in many cases, confusion has arisen from calling the normal glands gastric mucosa.

There also seems to be some question as to racial differences in the arrangement of some of the glandular elements. Gillman[5] states that while he has noticed groups of glands conforming to the cardiac pattern clustered under cover of the esophageal epithelium immediately above the junction, he has found it impossible to separate them from the true cardiac glands of the stomach. He believes that while cardiac glands of the esophagus may exist in the European, as a separate entity, in the South African Negro (Bantu) there is no real evidence for separating the glands into an esophageal and a stomach group.

Because of the relatively meager information in the literature and in view of the above discrepancies, we undertook to study the histology of the cardioesophageal junction with special reference to the glandular structures. To this end, sections of this area were prepared from 72 consecutive routine autopsies at the U. S. Veterans' Hospital, Wood, Wis., and the following observations were made:

In the esophagus at the cardioesophageal junction, three types of glandular structures may be seen: the cardiac glands, the esophageal glands and an occasional area of the fundic glands of true gastric mucosa (see Fig. 1).

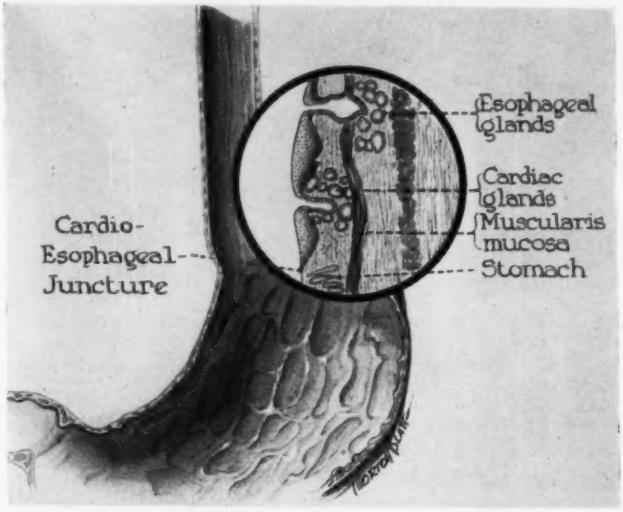

Fig. 1. Schematic drawing showing location of cardioesophageal glands.

The cardiac or superficial glands are found in the mucosa above the muscularis mucosa (see Figs. 2 and 3). They are of a branched tubular variety with a pale cytoplasm. Their ducts are composed of one layer of high columnar cells, having a characteristic palisade appearance. These glands are found in the esophagus within a centimeter or two above the stomach and in the cardia from which they derive their name. Sometimes they are directly connected with similar glands on the stomach side and at others they are completely separated, with their ducts opening through erosion-like areas in the stratified epithelium of the esophagus. These glands at times seem to push the squamous epithelium aside, thus thinning it out. At any rate, our sections indicate that these glands are definitely a part of the esophagus rather than elements of

Fig. 2. Cadiac glands: Embedded in epithelium (×400).

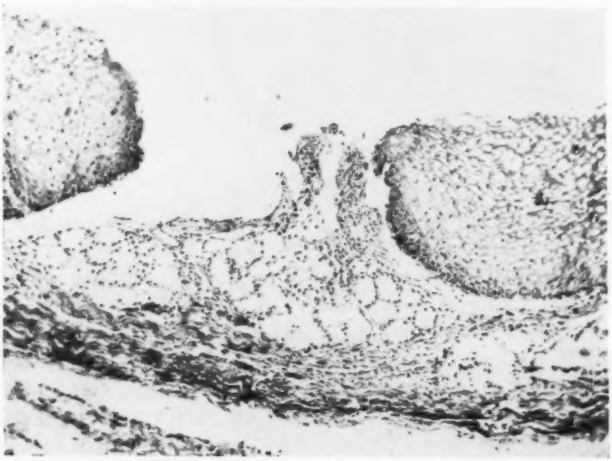

Fig. 3. Cardiac glands: Outlet in esophageal epithelium (×140).

stomach glands, which appear to be in the esophagus because of angles of sectioning in the preparation of the slides, or just a crowding over the border of an essentially stomach struc-

ture. Furthermore, these glands have been reported in the upper portion of the esophagus as a fairly constant phenomenon.

Occasionally acid parietal cells were found attached to the periphery of the lobule of the cardiac glands. These cells have also been found by other investigators.[4] They are relatively few in number and could not account for any appreciable amount of acid.

Johnson[6] believes that this type of gland is embryologically different from the mucous or esophageal glands and occurs first in the 12-week fetus, while the deep mucous type is found first in the 28-week fetus. Others believe that the two types of glands are of the same embryonic origin and that the superficial type develops earlier and is crowded down to form the deep glands.

The esophageal glands or deep glands are true mucous glands with a basophilic cytoplasm and are found beneath the muscularis mucosa only (see Fig. 4). These glands are of a tubuloalveolar variety. Their ducts are composed of a layer of pseudostratified cuboidal epithelium in the smaller radicals, and in the larger ducts one will find stratified squamous epithelium. Dilatations of these ducts are common and sometimes reach cystic proportions. Occasionally one can see acini with marked eosinophilic staining characteristics. These, however, do not have the typical appearance of serous glands and probably represent some stage in the glandular activity (see Fig. 5).

In regard to the presence of true gastric mucosa in the esophagus, we have found at least one section in which gastric mucosa, that is, actual fundic glands, are found under the stratified epithelium of the esophagus (see Fig. 6).

Much has been written concerning the etiology of the ulcerative lesions of the lower esophagus. By far the majority of investigators believe that the ulcers are caused and perpetuated by the irritating effect of acid. Our studies would seem to indicate that the acid-producing potential of the esophagus

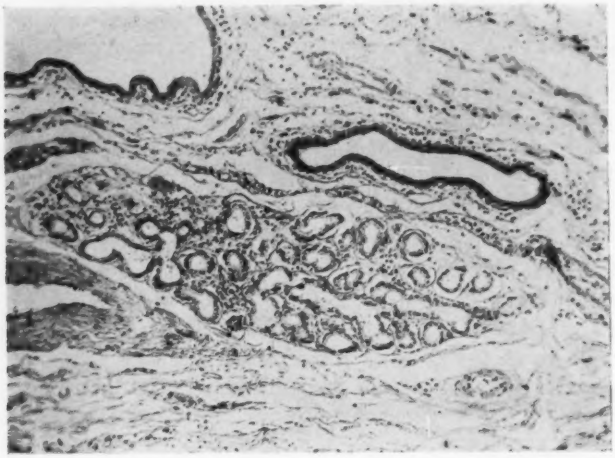

Fig. 4. Esophageal glands and ducts: Lying beneath muscularis mucosae (×140).

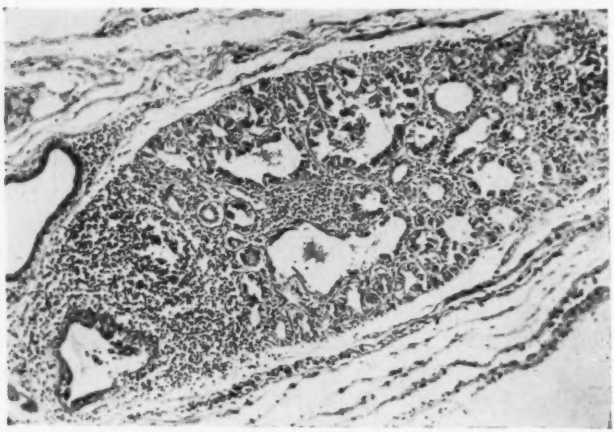

Fig. 5. Esophageal glands and ducts: Glands have a "serous" appearance (×140).

is minimal, considering the rare occurrence of gastric mucosa in the esophagus and the occasional parietal cells in the cardiac glands. Whatever acid may be found in the esophagus

undoubtedly is regurgitated from the stomach. The breaks in the stratified epithelium caused by the openings of the glandular ducts may be a source of ingress for infection or irritating acid. In spite of this, one of us[8] reported seeing active ulcerative lesions above strictures of the esophagus in two

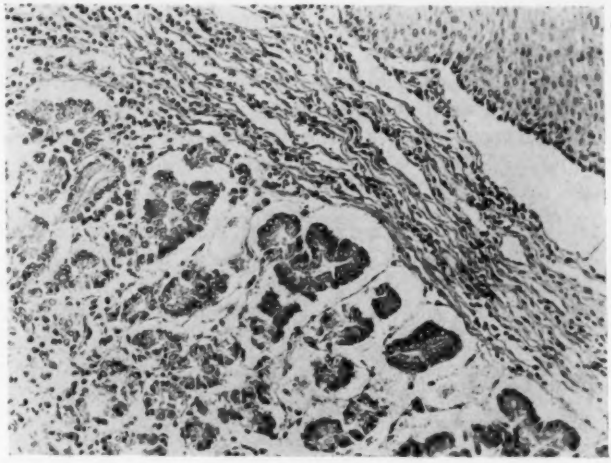

Fig. 6. Gastric glands: True gastric glands, comprised of chief and parietal cells lying under esophageal epithelium (×230).

patients whose gastric acidity had been greatly lowered, one by vagotomy and the other by gastric resection to the extent that the coexisting duodenal ulcers healed. It is a curious thing also that these ulcerations occur most commonly in cases of short esophagus, or other benign strictures. A large number of authors believe that these lesions are caused by the retraction circumferentially of the scars of these ulcers. In the case of the short esophagus, longitudinal retraction as well would cause pulling of the cardia into the chest. To my mind, there is still a definite question as to whether the ulcerative lesions of the lower esophagus are a cause or effect of inflammatory stricturing of the esophagus. Butt and Vinson[7] believe that true peptic ulcer of the esophagus does not occur and that these ulcerations, which are usually quite shallow, are but a phase of a nonspecific esophagitis.

Pathologists have also wondered what the relationship of these glands is to the development of malignancy in this area. McPeak and Warren[9] in studying 65 cases of carcinoma of the cardioesophageal junction found that adenocarcinomata which are frequently found in the lower portion of the esophagus seldom occur elsewhere in this organ. Information gained from a study of the literature and their own series indicates that the adenoacanthomas (a salivary gland type of tumor) and some of the papillary adenocarcinomata take their origin from the deep glands of the esophagus. Other papillary adenocarcinomata seem to take their origin from the cardiac glands.

SUMMARY.

Seventy-two cardioesophageal junctions of successive autopsy specimens were studied. Discrete nests of cardiac glands opening into the esophagus were found in many of the specimens. Submucous collections of mucinous esophageal glands with many dilated and cystic ducts were seen. One specimen showed an island of true gastric mucosa in the lower esophagus. There does not seem to be sufficient acid-forming cells in the esophagus to produce enough acid to account for ulceration; if acid is the cause, it must come from regurgitation. A possible origin for adenocarcinma or adenoacanthomata from those glands has been indicated.

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THE DIAGNOSIS AND TREATMENT OF ACUTE SUBDURAL ABSCESS COMPLICATING SUPPURATIVE FRONTAL SINUSITIS.*

WILLIAM REID PITTS, M.D. (by invitation),
Charlotte, N. C.

Acute subdural abscess complicating suppurative frontal sinusitis is a serious yet often overlooked entity. Although sporadic case reports of this disease have appeared in the literature for more than two centuries (DeLaPeyronie,[1] in 1699), accurate knowledge of its clinical symptomatology and pathogenesis is of relatively recent date and is credited to the work of Courville,[2] Kubik and Adams,[3] and Ray and Parsons.[4] Prior to the advent of the antibiotics this fulminating condition was almost invariably fatal and was rarely diagnosed during life. By adequate surgical drainage combined with the use of penicillin and sulfonamides, a number of cured cases have been reported in recent years: Gurdjian and Webster,[5] Schiller, Cairns and Russell,[6] Keith and McKenzie,[7] List.[8] It would, therefore, seem pertinent at this time to review the clinical picture and treatment of acute subdural abscess, in order that more of these cases will be recognized in the early phase of the disease at a time when surgery offers a reasonably good prospect of cure. Our experience with four successive cases during the past five years will also be reviewed. Tables I through VI depict the salient features of the cases in this series.

REPORT OF CASES.

Case 1: Frontal sinusitis and headache were present for one week. Swelling of the forehead and severe headache for five days was followed by sudden appearance of speech difficulty and right hemiparesis associated with vomiting for two days. Jacksonian seizures of the right side were followed by loss of consciousness and generalized convulsive seiz-

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ures associated with stupor, fever and leucocytosis. There was present a right hemiparesis, stupor, positive Babinski right, mild stiffness of the neck, swelling about both eyes and forehead. Spinal fluid showed pressure of 320 mm. of fluid, clear and colorless, 99 cells — 84 of the cells were polymorphonuclear leucocytes, 15 were lymphocytes. Immediate operation was carried out. Osteomyelitis of the frontal bone was found,

TABLE I

Case No.	Age	Sex	Organism	Site	Meningitis
1	15	M	Streptococcus. Failed to subculture.	Left Hemisphere Convexity.	No
2	15	M	Hemolytic Staphylococcus Aureus.	Left Hemisphere Convexity.	No
3	45	M	Gram Positive Cocci in Chains and Clumps. Culture - No Growth.	Left Hemisphere Convexity.	No
4	49	M	Micro-aerophilic Beta Streptococcus.	Left Hemisphere Convexity. Long. Fissure. Right Hemisphere Convexity.	Yes

TABLE II

Case No.	Duration of Sinusitis	Duration Neurologic Symptoms	C. S. F. Pressure	C. S. F. Cells	Blood W.B.C.
1	1 Week	2 Days	320 mm.	99	19,000
2	10 Days	2 Days	210 mm.	2970	24,000
3	6 Weeks	1 Day	460 mm.	3015	20,650
4	Chronic for years. Relapsing acute 5 Weeks.	14 Hours	250 mm.	1956	31,000

resected. Bilateral empyema of the frontal sinuses necessitated eradication of both. Following this, a large left subdural abscess was drained. The patient had a stormy postoperative course, frequent convulsions for two days, stupor for four days. There was complete recovery from the right hemiparesis and the speech defect; however, the patient has had intermittent generalized convulsive seizures as a residual sequela, which are well controlled by anticonvulsants.

J. D. A., a 15-year-old boy, was admitted to the Charlotte Memorial Hospital on Dec. 23, 1945, in a stuporous state, having continuous generalized convulsive seizures. Twelve days prior to admission to the hospital the patient was ill at home with what was called the flu, complained of frontal headache and had a nasal discharge. At this time he was able to be up and around the house a portion of the time. Five days prior to entry into the hospital the patient cried the entire day with severe pain over both eyes. On the following day his forehead was markedly swollen. Three days prior to admission both eyes were swollen completely shut.

TABLE III

SIGNS AND SYMPTOMS	No. of Cases
1. Suppurative Frontal Sinusitis	4
2. Headache	4
3. Fever (102.4° - 103.8°)	4
4. Jacksonian and Generalized Seizures	1
5. Jacksonian Seizures	2
6. Generalized Seizures	1
7. Nuccal Resistance	4
8. Right Hemiparesis and Aphasia	4
9. Stupor	4
10. Intracranial Hypertension	4
11. Pleocytosis	4
12. Blood Leucocytosis	4

TABLE IV

ROENTGENOGRAPHIC CHANGES	No. of Cases
1. Bilateral Frontal Sinus Clouding	2
2. Left Frontal Sinus Clouding	1
3. Right Frontal and Maxillary Sinus Clouding	1
4. Evidence of Osteomyelitis of Frontal Bone	0

TABLE V	No. of Cases
1. Necrosis of Posterior Plate of Frontal Sinus	1
2. Epidural Abscess	1
3. Brain Abscess Coexisting or Complicating	0
4. Meningitis Coexisting	1

TABLE VI

LOCAL & SYSTEMIC THERAPY WITH ANTIBIOTICS & SULFADIAZINE

Case No.	Subdural Penicillin	Intrathecal Penicillin	Intramuscular Penicillin	Strepto-mycin	Sulfadiazine	Terra-mycin
1	No	No	30,000 Units Q2H x 10 Days 20,000 Units Q3H x 3 Days 30,000 Units Q12H x 2 days	No	Sod. Sulfad. gm. 5 stat. 2.5 gm. Q6H x 3 Days 2 gm. Q6H x 2 Days 1.5 gm. Q4H x 2 Days 1 gm. Q4H x 4 Days	No
2	15,000 Units in 15 cc. x 2 Days 10,000 Units in 10 cc. x 5 Days	15,000 Units in 15 cc. x 5 Days	50,000 Units Q3H x 12 Days	No	Sod. Sulfad. gm. 2.5 Q8H x 6 Days 1 gm. Q4H x 6 Days	No
3	At Operation 10,000 Units in 10 cc. 10,000 Units in 10 cc. x 4 Days 5,000 Units in 5 cc. x 3 Days	15,000 Units in 15 cc. x 3 Days	200,000 Units Q3H x 6 Days 100,000 Units Q3H x 3 Days 50,000 Units Q3H x 5 Days	No	Sod. Sulfad. 2.5 gm. Q12H x 7 Days 1 gm. Q4H x 4 Days 1 gm. Q6H x 3 Days	No
4	No 100,000 Units in 10 cc. Daily x 7 Days in Epidural Space	No	100,000 Units Q2H x 7 Days 100,000 Units Q3H x 3 Days	1 gm. Pre-Op.	Sod. Sulfad. 4 gm. stat. 1 gm. I.V. Q4H x 2 Days 1 gm. I.V. Q6H x 3 Days 1 gm. Q4H x 2 Days 1 gm. Q6H x 6 Days	500 mg. I.V. Q6H x 6 Days 500 mg. I.V. Q12H x 2 Days

At this time the L. M. D. gave the patient penicillin and made a small 2 cm. incision in the middle of the forehead. On the following day the patient had difficulty naming objects, and it was noted that he had a weakness of his right upper extremity. These symptoms were associated

with vomiting and continuation of severe frontal headache. On the day of admission to the hospital there was profuse drainage of pus from the forehead incision. Eight hours prior to admission to the hospital the patient began to have Jacksonian seizures, starting in the right arm and face and extending to the right lower extremity and then after a few minutes the seizures became generalized, implicating the extremities bilaterally. The first seizure lasted five minutes, and following this he had a succession of seizures, only a few minutes apart, until he had had four convulsions in a period of six hours. When brought to the hospital the patient was in a stuporous state, having frequent convulsions originating in the right face and arm and then spreading to become generalized.

The temperature was 103.8° (rectally), pulse 86, blood pressure 160 systolic and 60 diastolic. The patient was having frequent convulsive seizures, which were controlled with some difficulty by means of intravenous sodium luminal. Between convulsions he was stuporous and did not resist noxious stimuli. The pupils were small, contracted, equal and reacted to light bilaterally. Both optic fundi showed engorgement of the retinal veins but no papilledema. There was present a flaccid right hemiparesis of rather severe degree. There was an extensor plantar response on the right side as well as absent abdominal reflexes on the right. There was slight nuchal rigidity. Pus was observed in the left middle meatus of the nose. Periorbital swelling was obvious and the entire forehead was swollen, boggy and edematous. The edema of the scalp extended back to the coronal suture. In the center of the forehead was a 2 cm. vertical incision which was draining thin yellow pus.

The blood leucocyte count was 19,000, with 88 per cent polymorphonuclear leucocytes, 10 per cent lymphocytes, 1 per cent eosinophile, and 1 per cent monocyte. A lumbar puncture revealed the cerebrospinal fluid to be grossly clear and colorless, with a pressure of 320 mm. of fluid; the cell count was 99 cells per cm. (84 of the cells were polymorphonuclear leucocytes, and 15 were monocytes); the total protein content was 49 mg. per hundred cc., globulin was negative, and the sugar content was 40 mg. per hundred cc. Cultures of the fluid were sterile. Examination of the urine revealed a specific gravity of 1.020, pH 6.0, a trace of albumin, and an occasional R. B. C. and W. B. C.

Immediately on admission to the hospital the patient was given 40,000 units of penicillin intramuscularly, 1,000 cc. of 5 per cent glucose and saline, with 5 gm. of sodium sulfadiazine. The convulsive seizures were brought under control by administration of 4 gr. of sodium luminal intravenously.

Three and one-half hours after admission to the hospital, operation was carried out as an emergency procedure for resection of a portion of the frontal bone, eradication of both frontal sinuses, and drainage of an acute left subdural abscess. A coronal incision was used and the scalp was reflected forward to the orbital ridge bilaterally. In the midfrontal region it was found that the periosteum had been detached from the bone for an area 5 by 7.5 cm., extending from the region of the right supraorbital ridge and running upward and backward to the left in an oblique manner. This cavity was lined by a fibrinous exudate and communicated with the midline incision on the forehead. The denuded bone was rough and was obviously the seat of osteomyelitis. A burr hole was made in the involved osteomyelitic bone and all of the bone which had been found to be denuded was resected. The supraorbital ridge was preserved on both sides. The frontal sinuses were opened bilaterally from

above and both sinuses were found to be filled with thick creamy pus. The mucous membrane of the left frontal sinus was found to be completely necrotic. Both frontal sinuses were obliterated completely. On the surface of the dura behind the posterior plate of the left frontal sinus, about 4 cm. from the midline, was an area of inflammation with a rather heavy exudate on the surface. The granulation plaque was 1.5 cm. in diameter, and from the center of the plaque exuded several droplets of pus. Upon enlarging this pinpoint opening in the dura, 2 cc. of pus were found in this area. The brain was exceedingly tight, and the cortex tended to herniate. It was, therefore, obvious that the patient had a further collection of pus elsewhere. A burr opening was then made and enlarged slightly in the left frontotemporal region. Upon opening the dura, 60 to 75 cc. of thick yellow pus came away under tension from the subdural space, the collection being greatest in the left temporal region. Immediate smear of the pus revealed numerous disintegrated pus cells, with very few Gram positive cocci. Culture of the pus showed Gram positive cocci in chains which failed to subculture aerobically or anaerobically. By depressing the cortex with a brain spoon the pus was allowed to escape, and the subdural space was washed out with saline. The surface of the brain was covered with a thick plastic exudate and on the underneath surface of the dura a similar filmy membrane was noted. The subdural space was adequately irrigated between the burr openings in the frontal and temporal region. Upon removal of the pus from the subdural space in the temporal region, intracranial tension was immediately reduced and the brain did not herniate further. In order to define the posterior limits of the abscess, another burr hole was made in the left posterotemporal region. There was no evidence of suppuration or reaction over the cortex of the brain at this level, and this wound was closed immediately. The coronal incision was then closed with interrupted fine black silk sutures, one rubber tissue drain was left in the epidural space in the region of the frontal sinuses, and a small rubber tissue drain was left in the left subdural space extending down to the temporal lobe of the brain. The patient's general condition had improved considerably by the time the procedure had been completed.

The patient's postoperative course was stormy for a period of four days. Jacksonian seizures implicating the rightsided extremities and the face were troublesome for a period of 48 hours. The stupor gradually lightened, and on the fourth day postoperatively the patient was able to follow commands. He took sufficient nourishment to maintain a normal balance 11 days postoperative, after having had gastric tube feedings over a period of eight days. The fever gradually subsided over a span of seven days. On the third postoperative day, lumbar puncture revealed a clear, colorless, cerebrospinal fluid under normal pressure with a cell count of one neutrophile and 10 lymphocytes. The subdural drain was removed on the third postoperative day and the epidural drain on the eighth postoperative day.

Postoperative treatment consisted of adequate fluids parenterally to maintain a normal fluid balance, a transfusion of 300 cc. of blood on the third postoperative day, and the administration of penicillin and sulfadiazine systemically as indicated in Table VI.

Throughout the postoperative period the patient's neurologic signs improved, and by the time the patient was discharged from the hospital on Jan. 12, 1946, his twentieth postoperative day, the dysphasia and the right hemiparesis had completely cleared up, the wound had healed by primary intention, and the patient was without symptoms.

Three weeks following discharge from the hospital the patient had a generalized convulsive seizure, which was followed by a second one a month later. Neurologic examination was negative at that time and anticonvulsant therapy was begun. The convulsive state has remained under control by the administration of phenobarbital and dilantin sodium.

July 10, 1946, the patient was readmitted to the Charlotte Memorial Hospital, at which time the cranial defect was repaired by means of a tantalum plate (see Fig. 1). Again the wound healed by primary intention, and the patient was discharged home on the sixth postoperative day. In the Fall the patient resumed his school activities and, upon finishing the term, became gainfully employed. The patient has not had any convulsive seizures in 10 months.

Fig. 1. Case 1. Recent photographs showing little or no deformity of the frontal region.

Comment: This case represents the typical course of an acute suppurative frontal sinusitis which rapidly spread to produce an osteomyelitis of the frontal bone and direct penetration of the dura to form an acute subdural abscess without perforation of the posterior plate of the frontal sinus. Speech disturbance, a right hemiparesis, and finally Jacksonian seizures progressing to generalized convulsive seizures, along with stupor, fever and toxicity, heralded the intracranial complication. Cure was effected by prompt surgical drainage of the acute subdural abscess, radical resection of the involved frontal bone, complete eradication of both frontal sinuses, and systemic administration of penicillin and sulfadiazine.

In spite of the fact that no penicillin was injected into the subdural space, the patient was left with a generalized convulsive state as a sequela, which is well controlled on adequate anticonvulsant therapy.

Case 2: Acute frontal sinusitis and headache were present for 10 days. There was improvement on the administration of penicillin and streptomycin elsewhere for one week. Following the discontinuance of chemotherapy, within 24 hours, there was a recurrence of the severe pain over the left eye, fever, leucocytosis, mental confusion, trauma, signs of acute suppurative frontal sinusitis, slight rigidity of the neck, and right hemiparesis. The cerebrospinal fluid showed initial pressure of 100 mm. of water, and cell count of 297 with 90 per cent polymorphonuclear leucocytes. X-rays of the sinuses revealed definite clouding in the left frontal sinus with a maxillary sinus on the same side completely radiopaque. A radical external frontal sinus operation revealed bilateral empyema of the frontal sinuses. The dura was rather dull and tense in the left frontal region. Sixteen hours later the cerebrospinal fluid pressure was 200 mm. of fluid and showed 2,970 cells, almost all of which were polymorphonuclear leucocytes. There was a marked weakness of the right arm, and the patient was having frequent Jacksonian seizures implicating the right face and right upper extremity. An acute subdural abscess over the left cerebrum was drained through two enlarged burr holes and the patient gradually recovered with massive therapy consisting of intramuscular penicillin, irrigation of the subdural space with penicillin solution, and intravenous sodium sulfadiazine. The convulsive seizures were a difficult problem in the immediate postoperative period and generalized convulsive seizures remained as a sequela, although they are under control with appropriate anticonvulsant therapy.

C. R. B., a 15-year-old school boy, was admitted to the Charlotte Eye, Ear and Throat Hospital, Nov. 17, 1949, in a semistuporous state because of pain over the left eye, and fever. Ten days previously he complained of pain over the left eye. The following day he was hospitalized elsewhere because of redness and swelling about the left eye; he was given penicillin and streptomycin. Upon improvement, he was discharged one week later. Within 24 hours there was a recurrence of severe pain over his left eye and his fever rose to 103°. For 24 hours previous to admission, the parents noted that he was gradually becoming lethargic, stuporous and irrational.

The temperature was 101.6° F. (rectally), the pulse rate 110, and the blood pressure 126 systolic and 40 diastolic. He was extremely lethargic but could be aroused to cooperate and appeared acutely ill. He responded to pressure over the left frontal sinus, which was dark to transillumination. There was frank pus in the left middle meatus. Irrigation of the left antrum through the inferior meatus yielded thin pus. Kernig's sign was positive and there was slight nuchal rigidity. The fundi were normal.

Immediate lumbar puncture revealed a grossly clear fluid with a pressure of 100 mm. of water. The C. S. F. cell count was 297 white cells per cm., 90 per cent of which were polymorphonuclear leucocytes. The blood leucocytes numbered 24,000 per cm., with 85 per cent polymorphonuclear leucocytes and 15 per cent lymphocytes. Roentgenograms of the sinuses revealed the fact that the right frontal sinus showed some density along the inner half. The left showed a radiopacity except a small space about 0.5 cm. wide along the outer border. Both ethmoidal labyrinths were

radiopaque. The right maxillary and both sphenoid sinuses were normal. The left antrum was radiopaque (see Fig. 2A). Adequate systemic sulfadiazine and penicillin therapy was started on admission to the hospital. Neurosurgical consultation revealed, in addition to the above findings, a weakness of the right upper extremity and a slight dysphasia. It was felt that the patient had either an extradural or subdural abscess on the left side. It was agreed that the first thing to do was to eradicate the focus of infection in the left frontal sinus and at the same time rule in or out extradural abscess.

Fig. 2A. Case 2. Preoperative Roentgenogram of sinuses showing marked opacity left frontal, density of medial half right frontal, bilateral radiopaque ethmoid cells, and clouding left maxillary sinus.

A radical external frontal sinus operation was done immediately. All of the frontal floor and related ethmoidal cells were removed. Bilateral empyema of the frontal sinuses was found; however, there was no evidence of frank osteomyelitis. The entire anterior wall of the left frontal sinus and a part of the right anterior wall was removed. The dura was widely exposed by removal of the posterior plate in its entirety on the left and partially on the right. No evidence of an epidural abscess was encountered, nor was there any necrosis of the posterior plate. The dura in the left frontal area was dull in appearance and was tense. The field was packed with iodoform gauze with exit out the left nasofrontal duct. Primary closure was done with silk interlocking and mattress sutures.

For 16 hours following the sinus operation the patient progressively grew worse. He became more stuporous. The right arm paresis became more marked, the fever rose to 103°, and finally the patient began to

have tonic clonic convulsive movements of the right face and right arm. Lumbar puncture then revealed the cerebrospinal fluid under pressure of 210 mm. of water, cell count being 2,970, practically all polymorphonuclear leucocytes. Because a subdural abscess was suspected, he was transferred to the Charlotte Memorial Hospital promptly (Nov. 19, 1949) for immediate operation.

On admission to the Charlotte Memorial Hospital (Nov. 19, 1949), the temperature was 103.8° F., the pulse rate 90, and the blood pressure 130 systolic and 46 diastolic. He was completely stuporous and having almost continuous Jacksonian seizures implicating the rightsided extremities and the right face. The pupils were equal and reacted to light and accommodation. Both optic fundi showed engorgement of the retinal veins, but papilledema was not present. There was present a right hemiparesis of marked degree, being most noticeable in the right upper extremity. The deep tendon reflexes on the right side were sluggish. The Babinski sign was present on the right.

Operation was carried out promptly on admission to the Charlotte Memorial Hospital, and through two enlarged burr openings a large left subdural abscess was drained. One burr opening was made in the frontal region just anterior to the hair line, and the other in the posterior frontal region about 4 cm. from the midline. The subdural space was carefully washed out with saline. The arachnoidal surface of the brain was coated with a thick plastic exudate, which was dull in appearance. Three soft rubber catheters were introduced into the subdural space and left in situ for future irrigation with penicillin. The tip of one was left in the parietal region, one in the temporal region, and a third near the frontal pole of the left hemisphere. After the two incisions had been closed, 5 cc. of saline containing 5,000 units of penicillin were instilled into each of the three catheters left in the subdural space.

Culture of the pus removed from the subdural space revealed a pure culture of hemolytic staphylococcus aureus. Cultures of the cerebrospinal fluid were negative.

The immediate postoperative period was extremely stormy, and for three days Jacksonian seizures, implicating the right face, arm and leg, were very difficult to control. The stupor persisted for five days; however, on the sixth postoperative day the patient was sufficiently alert to take adequate fluids by mouth to maintain a normal balance. Gradually over a period of six days, the fever subsided. The postoperative therapy consisted of general supportive measures including whole blood, transfusions, adequate fluid parenterally to maintain a normal balance. The details of the local and systemic administration of penicillin and sulfonamides is depicted in Table VI.

Forty-eight hours following the operation, the patient's neurologic status began to improve, and improved steadily thereafter. At the time of discharge from the hospital on Dec. 11, 1949 (twenty-second postoperative day), the patient's right hemiparesis and dysphasia had completely cleared up, and he was asymptomatic.

One month following discharge from the hospital the patient re-entered high school, and five months later he returned for a left frontal cranioplasty, at which time the defect in the left frontal bone was repaired with a tantalum plate (see Figs. 2B and 3). Six months following his illness the patient had a generalized convulsive seizure. In spite of adequate anticonvulsant therapy the patient experienced a second generalized con-

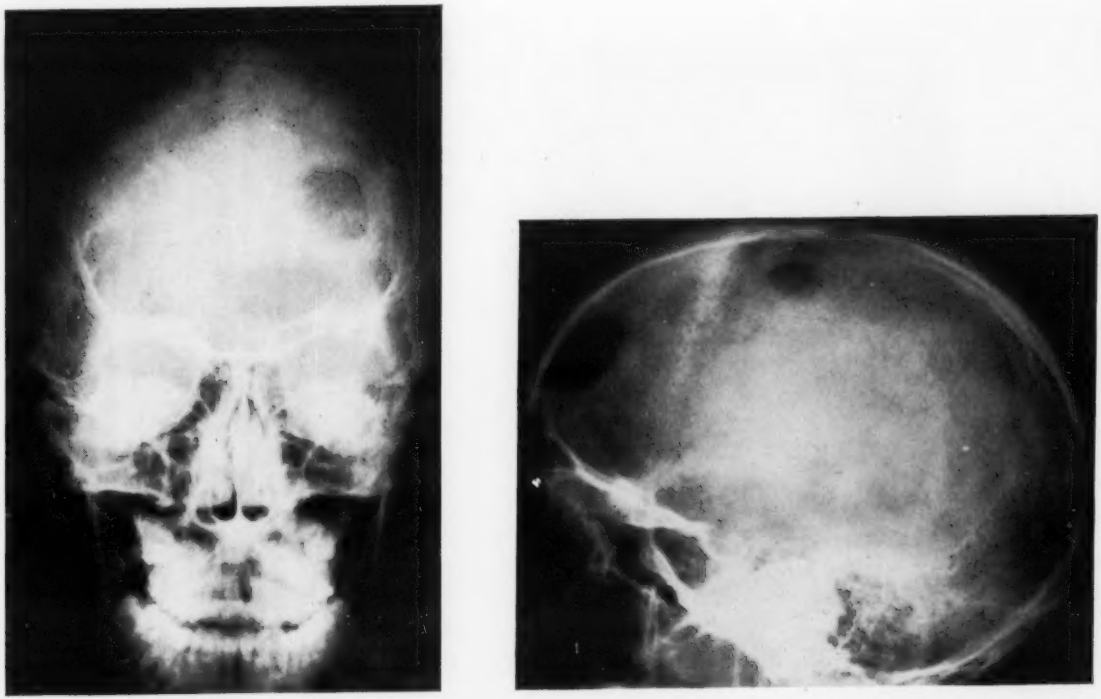

Fig. 2B. Case 2. Postoperative skull Roentgenograms depicting extent of bone removal in the frontal region and the site of burr openings for drainage of the subdural abscess.

vulsive seizure three months later. The patient's generalized convulsive state has remained well controlled on dilantin sodium and phenobarbital therapy, inasmuch as he has not had any further generalized convulsive seizures in the past 15 months. Occasionally he has a light psychomotor seizure lasting three to five minutes. Patient is now operating a small grocery store, having finished his school work.

Fig. 3. Case 2. Recent photographs showing little or no deformity of the frontal region.

Comment: This patient apparently had an acute suppurative frontal sinusitis which was temporarily benefited by chemotherapy; however, immediately upon cessation of chemotherapy the infection became rampant and a subdural abscess promptly developed. The lack of frank osteomyelitis at the time of operation and the lack of evidence of direct invasion of the dura suggest very strongly that the infection to the subdural space was by way of the venous channels. Eradication of the primary focus of infection, followed by prompt drainage of the subdural abscess with adequate penicillin and sulfadiazine, resulted in a cure. Previous to the sinus operation the possibility of an extradural abscess was very strongly entertained, and had we been entirely sure that the intracranial infection was in the subdural space, the two operative procedures could have been combined on the first day instead of draining the subdural abscess on the second day.

Case 3: Acute suppurative right frontal sinusitis was present three days, for which a Lynch type of external frontal sinus operation was done on the right side. Two weeks later, because of persistent infection, the anterior walls of both frontal sinuses and the posterior plate of the right frontal sinus were removed. Because of persistent severe left frontotemporal headache and fever, present for one week, patient was admitted to the hospital for the third time. Stupor, fever, nuchal rigidity, right hemiparesis, dysphasia, intracranial hypertension, pleocytosis, leucocytosis and finally rightsided Jacksonian seizures were present. Penicillin and sulfadiazine were administered in large doses, and a left subdural abscess was drained promptly. Recovery was gradual, and on the sixteenth postoperative day the posterior plate of the left frontal sinus, which showed osteomyelitis, was removed. The patient has remained well except for an occasional Jacksonian seizure, which is now controlled with anticonvulsant drugs. Cranioplasty is contemplated in the near future.

L. B. D., a 45-year-old man, was admitted to the Charlotte Eye, Ear and Throat Hospital on Dec. 17, 1950, because of swelling over the forehead and periorbital edema of two days' duration. Nine days previously the patient had consulted his local family physician for what was called an "ordinary cold." One week later he was seen by his family physician because of swelling over the forehead, edema about the eyes, and was hospitalized in his home town for sulfadiazine and penicillin therapy. Two days later, he was admitted to the Charlotte Eye, Ear and Throat Hospital because of suspected frontal sinusitis and osteomyelitis of the frontal bone.

The temperature was 100.4° F. (P. O), the pulse rate 90. The pertinent physical findings related only to the sinuses. Swelling and exquisite tenderness was present over the right frontal area. There was slight edema of the upper eyelids. Thick pus was present in the right middle meatus together with some polypoid tissue about the frontal duct. Foul smelling pus was washed from the right antrum through the inferior meatus.

The blood leucocyte count was 12,840, with 79 per cent polymorphonuclear leucocytes, eosinophile 1 per cent, monoctye 2 per cent. Roentgenograms showed unquestioned involvement of the right frontal sinus and antrum. The left sinuses appeared normal (see Fig. 4A). The cerebrospinal fluid was clear, with a cell count of 10.

A preliminary right intranasal antrum with conservative right ethmoid and sphenoid operation was done on Dec. 19, 1950, under local anesthesia. A polypoid right middle turbinate was removed. The following day a Lynch type of external frontal sinus operation was done on the right side. The sinus contained necrotic mucous membrane and pus. A counter-incision was then made up and to the left, exposing the anterior wall of the right frontal. There was no frank abscess or apparent bony necrosis. It was the opinion of the operator (V. K. H.) that he was dealing with a periostitis rather than a true osteomyelitis. Primary closure was then done with mattress and interlocking silk sutures; one iodoform pack was left in situ with exit out the right nasofrontal duct. Penicillin and aureomycin therapy had been started previous to operation and were continued postoperatively in a dosage of 400,000 units of penicillin S-R daily for nine days and 250 mg. of aureomycin every six hours for eight days. He was dismissed from the hospital on the seventh postoperative day.

One week later the patient returned because of persistent drainage from the wound. On admission to the hospital his fever was 101.4° and his leucocyte count was 16,240.

Fig. 4A. Case 3. Preoperative Roentgenogram depicting complete opacity right frontal sinus, slight density medial portion left frontal sinus, and clouding of right maxillary sinus.

The old incisions were reopened at a second operation. A left flap exposing the anterior wall of the left frontal sinus was obtained by an incision across the base of the nose. The anterior wall of each frontal sinus was removed. There apparently was little involvement of the left frontal. All of the posterior plate of the right frontal was removed. There was some apparent granulation tissue on the dura but no frank extradural abscess. The dura appeared normal beyond the confines of the sinus. The left nasofrontal duct was enlarged and one iodoform pack placed in each sinus with exit out to the nasofrontal duct. Because of the edema of the tissues, closure was done by mattress silk sutures tied over gauze.

In the immediate postoperative period he received 500 cc. of blood, and therapy consisted of 400,000 units of S-R penicillin intramuscularly daily for two days, aureomycin 250 mg. every six hours for two days, and

chloromycetin 250 mg. every six hours for eight days. The fever subsided by lysis in three days, and the patient was discharged from the hospital on his ninth postoperative day. Four days later the wound appeared to be edematous and the sutures were cutting through. The wound was now packed open with iodoform gauze. He was discharged, and Gantrisin was prescribed for home use.

Thirteen days later, on Jan. 29, 1951, he was readmitted to the Charlotte Eye, Ear and Throat Hospital because of fever and severe left frontotemporal headache, which had been persistent for one week. On admission to the hospital his fever was 103.4° F. (P. O.). The patient was lethargic, and there was some nuchal rigidity. The optic fundi showed venous engorgement and early swelling of the discs. The cerebrospinal fluid showed a cell count of 102 with 50 per cent polymorphonuclear leucocytes and 50 per cent lymphocytes. A blood leucocyte count was 13,000. Gantrisin and penicillin therapy was started immediately. His fever remained between 103° to 104°, and on the morning following admission he had a speech deficiency. He was transferred immediately to the Charlotte Memorial Hospital because of a suspected subdural abscess.

On admission to the Charlotte Memorial Hospital, Jan. 30, 1951, his temperature was 102.4° F. (P. R.), pulse rate 110, and the blood pressure 110 systolic and 70 diastolic. Patient was lethargic, dysphasic, and there was present muscular weakness of the right side, being most marked in the right upper extremity. Plantar response was normal bilaterally. The deep reflexes on the right side were diminished as compared to the left. There was moderate nuchal rigidity. The fundi showed venous engorgement with blurring of the borders of the discs. Lumbar puncture revealed cerebrospinal fluid, ground glass in appearance, under pressure of 360 mm. of fluid, with a cell count of 3,015, there being 95 per cent polymorphonuclear leucocytes and 5 per cent lymphocytes. Cultures of the spinal fluid were negative. The total protein of the cerebrospinal fluid was 170 mg. per cent, globulin 2 plus, sugar 63 mg. per cent, chlorides 680 mg. per cent. The blood leucocyte count was 20,650, 94 per cent polymorphonuclear leucocytes, 5 per cent lymphocytes. The urine examination revealed specific gravity of 1.019, pH 5.0, 2 plus albumin, negative sugar, R. B. C. per h. p. f. 1 to 2, W. B. C. per h. p. f. 1 to 2. It was not entirely clear whether we were dealing with a cerebritis or a subdural abscess; therefore, the patient was given 15,000 units of penicillin intrathecally in 15 cc. of distilled water, and was placed on sulfadiazine gm. 1 along with soda bicarbonate gm. 1 every four hours, as well as penicillin 100,000 units intramuscularly every three hours, and dihydrostreptomycin gm. 0.5 intramuscularly every six hours. Although the patient's temperature came down to 101.6° F. (rectally), and the pulse rate subsided to a level of 90, because of increased stupor and progression of the right hemiparesis, it was decided that burr holes should be made on the left side for a suspected acute left subdural abscess. While the head was being prepared for surgery, the patient for the first time had a right-sided Jacksonian seizure implicating the face and tongue. Lumbar puncture at this time revealed a cerebrospinal fluid with ground glass appearance, under pressure of 460 mm. of fluid. Fifteen thousand units of penicillin in 15 cc. of fluid were given intrathecally, and the patient was transferred to the operating room.

Exploratory trephination was carried out in the left frontal and temporal region on Jan. 31, 1951. The initial burr opening was made in the left posterior frontal region just anterior to the hair line. The dura was vascular and appeared whiter than normal. Upon incising the dura, thick

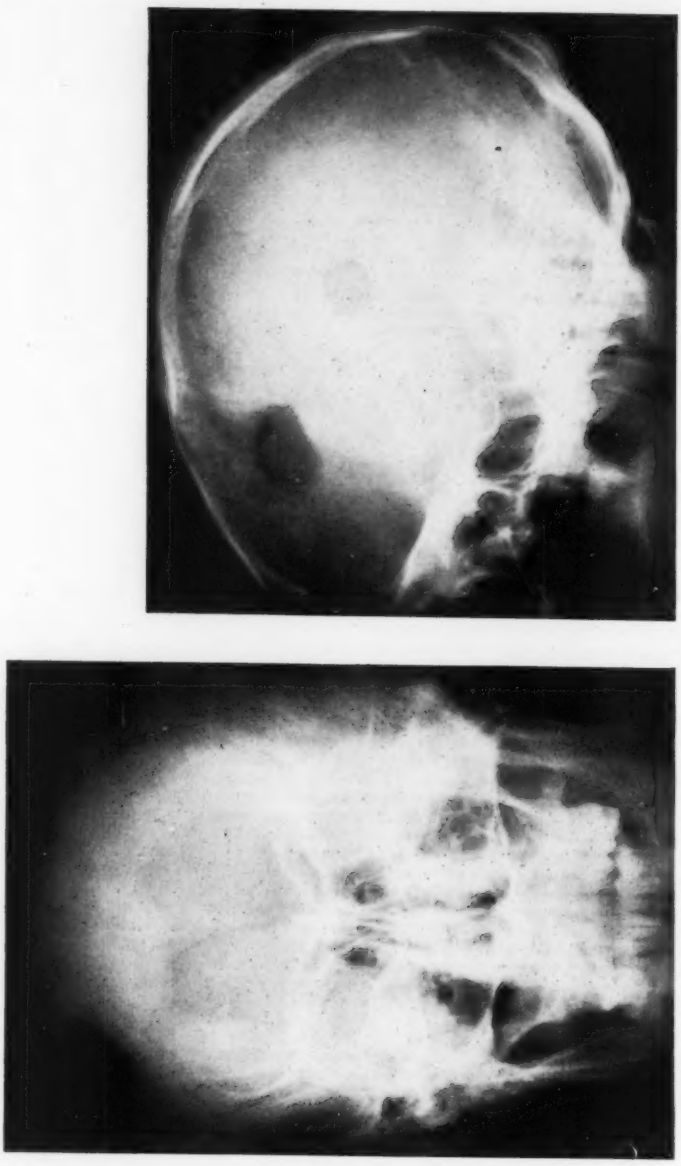

Fig. 4B. Case 3. Postoperative skull Roentgenograms depicting extent of bone removal in the frontal region and the site of burr openings for drainage of the subdural abscess.

greenish-yellow creamy, odorless pus exuded. Immediate smear of the pus showed Gram positive cocci in clumps and chains. Culture of the pus showed no growth. The burr hole was enlarged to the size of a 50-cent piece. The arachnoid was found to be thickened, and there were numerous fibrinous plaques over the exposed area. There was present a thin film of fibrinous tissue on the underneath surface of the dura. A considerable quantity of pus exuded; however, the brain was tight and tended to herniate, obstructing the drainage of the pus. In order to lower the intracranial pressure and to facilitate the irrigation of the subdural space, 30 cc. of fluid were removed from the lumbar thecal sac through the inlying spinal puncture needle. Following this maneuver the brain fell away from the dural edge and the subdural space was gently irrigated with warm saline solution through a soft rubber catheter. Irrigation was carried out until the returning fluid was completely clear. The subdural space was then irrigated with 90 cc. of a penicillin solution containing 90,000 units of penicillin. A second burr opening in the left temporal region, just anterior to the ear, did not reveal any pus; however, the arachnoid appeared to be somewhat thicker than normal. One catheter was left in the subdural space near the left frontal pole, and a second catheter was placed in the left parietal region for drainage and future instillation of penicillin solution. The wounds were closed, and 5,000 units of penicillin in 5 cc. of solution were instilled into each catheter.

There was steady improvement after operation. The stupor gradually lightened, and after 24 hours the patient was able to take small amounts of liquids by mouth. The hemiparesis gradually improved. The fever subsided by lysis in seven days. In 14 days the patient was sitting up, eating well, talking rationally; there was only a slight dysphasia; the motor power of the rightsided extremities was almost normal.

Postoperative therapy, other than general care, included administration of penicillin and sulfonamides as indicated in Table VI. On the fifth postoperative day the cerebrospinal fluid was grossly clear, with a pressure of 160 mm. of fluid, and a pleocytosis of only 30 cells, there being only six polymorphonuclear leucocytes and 24 lymphocytes.

In the immediate postoperative period, the control of convulsive seizures was somewhat of a problem. During the first five postoperative days the patient had Jacksonian seizures implicating the right face and upper extremity at irregular intervals, and on several occasions these progressed to generalized convulsions, necessitating the use of sodium pentothal intravenously. Sodium luminal was used to control the Jacksonian seizures. From the eleventh postoperative day the patient was free of convulsive seizures.

There was only a slight amount of drainage from the left frontal wound. One catheter was removed from the subdural space on the fourth postoperative day, and the second one was removed on the seventh postoperative day. Both cranial wounds healed by primary intention.

On the sixteenth postoperative day (Feb. 16, 1951) the remaining portion of the anterior wall, the posterior plate and the floor of the left frontal sinus were removed. The left frontal sinus was found to be filled with organizing granulation tissue and, on removing the posterior wall of the sinus, granulation tissue was found to be very adherent to the dura just to the left of the midline. Microscopic sections of the posterior plate of the left frontal sinus revealed chronic osteomyelitis with overlying ossifying periostitis.

On Feb. 27, 1951 (11 days following eradication of the left frontal sinus), a secondary closure of the granulating wound in the center of the forehead was carried out. The patient's recovery was uneventful, and he was discharged from the hospital on March 7, 1951, asymptomatic, without speech defect and with good motor power in his right-sided extremities.

The patient has remained well except for an occasional Jacksonian seizure implicating the right face and arm in a frequency of once every six or eight weeks, each seizure usually lasting a minute or two at a time. The first Jacksonian seizure occurred two months after discharge from the hospital. Since that time he has been controlled satisfactorily by the administration of anticonvulsant drugs. The patient is now gainfully employed, and is to return in the near future for a tantalum cranioplasty.

Comment: This case illustrates the fallacy of too conservative surgery in the face of suppurative frontal sinusitis. Antibiotics and sulfonamides cannot be expected to replace sound surgical principles, and should be used as an adjunct to surgery rather than a substitute for surgery. Although the original signs of sinusitis pointed to most marked involvement of the right frontal sinus, eventually necrosis of the posterior plate on the left developed, giving rise to an epidural and subdural abscess on the left. It is evident, from the pathology found at operation, that this patient had an osteomyelitis of the posterior plate of the left frontal sinus with direct extension of the infection through the plate and the dura, as evidenced by the granulations on the surface of the dura behind the posterior plate. Recovery was satisfactory following drainage of the subdural abscess, although it was necessary to postpone eradication of the focus of infection until a later date after the patient had recovered from the acute intracranial infection. This case illustrates the necessity of taking care of the acute subdural abscess primarily in those individuals where the condition of the patient is such that the eradication of the sinuses cannot be done at the same time and, therefore, must be postponed for a later date.

Case 4: For five weeks intermittent suppurative frontal sinusitis was treated elsewhere with antibiotics and sulfonamides. A sudden loss of consciousness and a generalized convulsion were followed by restlessness, stupor, fever, right hemiparesis, dysphasia, intracranial hypertension, pleocytosis, leucocytosis. Immediate operation revealed extensive subdural abscess over the convexity of the left cerebral hemisphere, bilateral suppurative frontal sinusitis, necrosis of the posterior plate of the left frontal sinus with an epidural abscess. The epidural and subdural abscesses were drained and bilateral frontal sinusectomy was car-

ried out in one sitting. Therapy included systemic use of penicillin, terramycin and sulfadiazine. Improvement was gradual for 16 days and almost complete when evidence of recurrence appeared. Mental confusion, fever, intracranial hypertension, pleocytosis, paralysis of the right foot led to drainage of pus from the longitudinal fissure on the left side. Death occurred 22 hours postoperatively. Autopsy showed a small collection of pus on the orbital surface of the left frontal lobe, a large right subdural abscess, organizing leptomeningitis over the frontal lobe, and focal hemorrhages in the pons.

E. F. C., a 49-year-old male, was admitted to the Charlotte Memorial Hospital on May 31, 1951, because of a recent convulsion. He had been troubled for a number of years with chronic sinusitis. Five weeks previous to admission the patient developed a sudden severe pain in the forehead, which was worse over the left eye. For one week he had constant frontal pain, and was treated for frontal sinusitis elsewhere. Four weeks prior to admission, the frontal sinusitis having apparently subsided, a polyp was removed from the patient's nose, and he returned to his work for one week even though there was some persistent tenderness over the frontal area. Three weeks prior to admission the patient had a flareup of his sinusitis, which was characterized by pain over the frontal region and particularly over the left eye. He was again put on chemotherapy, and remained in bed at home for two weeks with headache and low-grade fever. During this interval there was considerable swelling about the left eye and at one time the left eye was almost completely closed. Nine days previous to admission the symptoms had subsided, and the patient returned to work for one week. Thirty-six hours prior to entry the patient noted a feeling of tightness across his forehead, and 12 hours later the patient had to give up his work because of general malaise, fever (102°). Shortly thereafter, 20 hours previous to admission, he had a chill. An internist prescribed terramycin over the telephone. Two and one-half hours previous to admission the patient's wife noted that he was somewhat confused and was reluctant to talk. One hour previous to admission to the hospital the patient had a generalized convulsive seizure. Following the cessation of this convulsion the patient was in a wild, maniacal, restless, confused condition. A medical consultant administered 2 gr. of sodium luminal intramuscularly at home, and transferred the patient immediately to the hospital.

On admission to the Charlotte Memorial Hospital the temperature was 103° F. (P. R), pulse rate 100, respirations 32. Mild nuchal rigidity was present, and other than the wild, maniacal, restless, confused state, the neurologic examination was reported to have been negative. Patient was suspected of having meningitis. Immediate lumbar puncture revealed a slightly turbid cerebrospinal fluid under a pressure of 250 mm. of fluid; the cell count was 1,956 cells per cm. (95 per cent polymorphonuclear leucocytes and 5 per cent lymphocytes); the total protein content was 217 mg. per hundred cc., globulin 2 plus, sugar 95 mg. per hundred cc., and chlorides 682 mg. per hundred cc. Cultures of the fluid, reported later, showed microaerophilic beta streptococcus. Immediate therapy was initiated, consisting of penicillin, dihydrostreptomycin, and sodium sulfadiazine.

Neurosurgical consultation, six hours following admission to the hospital, revealed an acutely ill male. The patient was in a rather wild, restless, semistuporous state, thrashing about the bed. He was speechless and was unable to follow simple commands. There was present a weakness of the rightsided extremities and the right side of the face, the most marked involvement being in the right upper extremity. The

patient's hyperactivity made reflex examination unsatisfactory. Massive sedation in the form of 4 gr. of sodium luminal intramuscularly, 7.5 gr. of sodium amytal intravenously, and sodium pentothal gm. 0.5 intravenously were necessary to quiet the patient. Roentgenograms of the sinuses revealed small frontal sinuses which were cloudy bilaterally. Both antra showed the presence of discrete polyps. The left ethmoid appeared clear, but the right was somewhat hazy. Emergency operation was performed for a suspected acute subdural abscess secondary to bilateral, recurrent, acute suppurative frontal sinuisitis.

At operation, May 31, 1951, through a burr hole placed in the midparietal region on the left side, the dura appeared to be whiter than normal and under tension. The burr hole was then enlarged to the size of a 50-cent piece, and upon incising the dura there was an escape of odorless grayish-yellow thick pus. Immediate smear of the pus revealed numerous pus cells with Gram positive cocci in chains. Culture, reported later, revealed microaerophilic beta streptococcus. An estimated 100 to 125 cc. of pus was aspirated from the left subdural space and it seemed to cover the convexity of the entire left hemisphere. The subdural space was washed out with normal saline until the fluid returned clear. Following the cleansing of the subdural space, patient's general condition, which had been extremely precarious previous to the operation, improved. It was, therefore, decided that the focus of infection in the frontal sinuses could be eradicated at this time. The entire frontal bone was visualized by reflecting the scalp to the supraorbital ridge bilaterally by means of a coronal incision. The frontal bone showed evidence of osteomyelitis just above the supraorbital ridge, there being softening and discoloration of the bone. A burr hole was made on the left side just above the left frontal sinus. At the tip of the frontal pole, behind the posterior wall of the left frontal sinus, a collection of 15 cc. of pus was found in the epidural space. Granulation tissue was present on the dura in this area and droplets of pus exuded from a small opening in the middle of the area of granulation. An opening, 7 mm. in diameter, was found in the posterior plate of the left frontal sinus. Both frontal sinuses were found to be filled with thick creamy pus. The anterior wall of the left frontal sinus was soft and showed a honeycomb effect with pus. Pathological studies of the bone removed from the anterior and posterior wall of the left frontal sinus revealed chronic osteomyelitis. The anterior and posterior walls of the left and right frontal sinuses were completely removed, and the lining membrane stripped out. Drainage of the epidural space was had by bringing a soft rubber catheter from the frontal pole out through the temporal margin of the coronal incision. The subdural space was drained by two soft rubber catheters, one extending to the frontal pole, and the other into the left temporal region. At the end of the procedure the patient's general condition was much improved.

The postoperative course was rather stormy for four days and was marked by extreme restlessness; however, patient did not have any convulsive seizures. The schedule of the systemic administration of antibiotics and sulfonamides is shown in Table VI. No penicillin was injected into the subdural space, and there was very little drainage from the subdural catheters, which were removed on the fifth postoperative day. One hundred thousand units of penicillin in 10 cc. of solution were injected into the epidural space through the inlying catheter once daily for seven days. The stupor gradually lightened and the restlessness improved over a period of four days, at which time the patient was able to take fluids in quantity by mouth. On the fifth postoperative day the

patient talked for the first time, but a marked dysphasia was evident, as well as a moderate right hemiparesis. The fever cleared up by lysis over a period of seven days. On the fifth postoperative day the cerebrospinal pressure was 80 mm. of fluid; the cell count was 110, with 80 per cent polymorphonuclear leucocytes and 20 per cent lymphocytes.

The wounds healed by primary intention, and the dysphasia and right hemiparesis gradually improved over a span of 16 days. The patient was ready for discharge from the hospital and had been allowed on the campus of the hospital for two days when signs of recurrence appeared. On the sixteenth postoperative day, six days after the penicillin had been discontinued and three days after discontinuance of the sulfadiazine, there was noted some slowing of the mental processes of the patient, and while eating lunch, he suddenly developed a marked temporary paresis of the rightsided extremities for a period of two hours. On the following day the patient was more lethargic, was restless, and his temperature was 100° F. (P. O.). Examination at this time revealed that the patient alternated between lethargy and restlessness but was oriented for time and place. He was able to name objects satisfactorily. There was present a mild right hemiparesis, the lower extremity being involved more than the upper and the right foot was completely paralyzed. The fundi did not show any papilledema. Babinski sign was not present. The scalp over the bony defect in the frontal region was full and did not pulsate. The blood leucocyte count was 24,600, there being 82 per cent polymorphonuclear leucocytes, 8 per cent stab forms, 8 per cent lymphocytes, 2 per cent eosinophiles. Lumbar puncture revealed a faintly turbid cerebrospinal fluid, under a pressure of 370 mm. of fluid, with pleocytosis of 1,957, 95 per cent polymorphonucleor leucocytes, 5 per cent lymphocytes. In view of the presence of intracranial hypertension, signs of infection, and the progressive hemiparesis implicating primarily the right foot and lower extremity, we were led to believe that the patient had a collection of pus in the longitudinal fissure on the left side; therefore, penicillin and sulfadiazine therapy was resumed and immediate operation was carried out. Burr holes were made in the posterior frontal, anterior parietal and posterior parietal regions, about 2 cm. to the left of the midline. The dura in the frontal region was found to be white and somewhat thickened, and upon incising the dura a small collection of pus was found along the longitudinal fissure. When the left hemisphere was retracted laterally, pus welled up from between the hemispheres. The subdural space along the longitudinal fissure was irrigated with warm saline. Pus was also obtained in small quantities through the anterior parietal burr hole. In this area there was thickening of the dura and there was considerable fibrinous exudate on the cortex of the brain. The posterior parietal burr hole, which was 5 cm. anterior to the occipitoparietal suture line, revealed no evidence of pus or exudate on the surfaces of the brain. In order to afford more adequate drainage of the longitudinal fissure, the burr hole incisions were joined together, and a block resection of bone 11 cm. long and 3 cm. wide was carried out, extending from the posterior parietal region to the midfrontal region. The dura was opened through the extent of this incision except for the point of entrance of the rolandic veins to the longitudinal sinus. To facilitate the irrigation of the subdural space, 15 cc. of cerebrospinal fluid were removed from an inlying lumbar puncture needle, which collapsed the hemisphere, thereby making the irrigation much more effective. A small No. 8 soft rubber catheter was left in the interhemispheral space for drainage and for immediate instillation of penicillin. The amount of pus found between the hemispheres was small and the pockets were definitely less extensive than what had been anticipated preopera-

tively. At the end of the procedure the brain was still tight, which led us to suspect that the patient still had an undisclosed pocket of pus intracranially; however, his general condition was so poor at this time that it was felt that further exploration was unjustifiable.

The patient did not improve postoperatively. He remained comatose. Fever arose to 103.6° F. (P. R.), pulse 130, respirations 36 and labored. The scalp in the region of the bony defect in the left frontal area was bulging. In view of the persistent intracranial hypertension, the right hemiplegia, the possibility of a left frontal lobe abscess was entertained and the left frontal lobe was tapped, but no pus was found. Lumbar puncture revealed a cloudy field, under 320 mm. of pressure, with a cell count of 1,600, 98 per cent polymorphonuclear leucocytes. Patient died a respiratory death 22 hours following second operation.

At autopsy no evidence of infection was found in the region of the previously ablated frontal sinuses or the epidural space. The sphenoid and ethmoid sinuses were found to be normal. On the anteroinferior medial aspect of the left frontal pole a collection of approximately 12 cc. of greenish-yellow pus was found, and approximately 60 cc. of similar purulent material was found over the convexity of the right frontal, parietal and temporal lobes. There was thickening and slight hyperemia of the leptomeninges of the convexity of the right hemisphere from the frontal pole to the parietal area, including the right temporal lobe. A similar situation was found over the medial portion of the left frontal lobe for an area of about 3 cm. There was little or no thickening of the meninges elsewhere over the anterior portion of the left frontal lobe. The cerebral gyri were slightly flattened and the intervening sulci slightly narrowed, most conspicuously over the right hemisphere anteriorly. There was no gross evidence of temporal lobe or cerebellar herniation. There was no evidence of thrombosis of the cortical veins or the longitudinal sinus. Microscopic studies taken from the frontal lobes revealed an organizing leptomeningitis. There was no evidence of areas of cerebral softening. Punctate and focal hemorrhages were found in the pons. The lungs showed a bilateral bronchial pneumonia, lower lobes.

Comment: This is an example of acute suppurative frontal sinusitis superimposed upon a chronic frontal sinusitis which was improved with chemotherapy; however, there was recurrence of the infection on two occasions upon cessation of the chemotherapy. Osteomyelitis of the frontal bone finally developed, with erosion of the posterior wall of the left frontal sinus and the formation of an epidural abscess with extension of the infection directly through the dura to form a left subdural abscess. The prompt drainage of the left subdural abscess gave temporary relief of signs and symptoms; however, a persistent small collection of pus on the inferior medial aspect of the left frontal pole led to the extension of the infection up through the longitudinal fissure beneath the falx cerebri and over the right cerebral hemisphere. Although the

intrahemispheral collection was recognized and drained, failure to recognize the presence of the collection over the right hemisphere led to persistent intracranial hypertension, giving rise to petechial hemorrhages in the pons, resulting in death. This case serves to emphasize the fact that certainly bilateral frontal burr holes should be done in all patients suspected of harboring a subdural abscess, if the suspected side does not yield sufficient pathology to explain the syndrome, and, possibly, in all cases of subdural abscess even though sufficient pathology is found on one side to explain the syndrome.

The cranial subdural space is a potential space, just as the pleural and pericardial cavities are potential spaces. It is bound on one side by the dura mater and on the other by the arachnoid. Subdural abscess consists of a collection of purulent material in the subdural space overlying one or both cerebral hemispheres. Large collections of exudate are most likely to occur over the dorsolateral surfaces of the cerebral hemispheres because of the absence of any anatomic structures traversing the subdural space in that area. Pus that collects in the subdural space over one cerebral hemisphere tends to remain limited to one side; however, under pressure the fluid may cross to the opposite side via the subdural space in the longitudinal fissure; *i.e.*, under the falx cerebri, as in Case 4 of this series. Schiller, Cairns and Russell,[6] Keith and McKenzie,[7] and more recently List,[8] have shown that interhemispheral suppuration is far more common than previously realized.

PATHOGENESIS.

Acute pyogenic infection of the subdural space may develop either by direct or indirect route. In the first instance, a neighboring suppurative process extends directly through the dura. Suppurative frontal sinusitis, therefore, may lead to osteomyelitis of the posterior wall of the frontal sinus with necrosis of bone, formation of an extradural abscess and, finally, to subdural abscess, with or without actual perforation of the dura. An example of this mode of spread is seen in Case 4 of our series. The indirect vascular route of infection is probably more common. In severe suppurative frontal

sinusitis, thrombophlebitis of mucosal or orbital veins may develop and continue into the diploe of the skull, dural veins and sinuses, and finally into cerebral veins. Due to the exposed course of some of the dural and cerebral veins in the subdural space the formation of the subdural abscess is not unlikely. Once the infection has reached the subdural space it usually spreads rapidly over the convexity of the cerebral hemisphere without meeting obstacles and may extend from the frontal to the occipital pole. Under pressure, over a period of time, it is apt to invade the longitudinal fissure and extend beneath the falx to the other side. List[8] called attention to the fact that this was especially apt to occur when the purulent process originates at the orbital surface of the frontal pole. Case 4 in our series demonstrates the spread to the longitudinal fissure and the opposite hemisphere from a residual pocket on the orbital surface of the frontal pole. Thus, acute subdural abscess, secondary to suppurative frontal sinusitis, develops progressively in an anteroposterior direction, affecting either the dorsolateral surface of the hemisphere or the longitudinal fissure, or both regions.

The common infecting organisms in acute subdural abscess are usually the ones found in other intracranial infections arising from sinusitis, namely, pneumococcus, streptococcus, staphylococcus and influenzae bacillus. The causative organisms in our four cases were streptococcus and hemolytic staphylococcus aureus (see Table I).

CLINICAL SYMPTOMS, SIGNS AND DIAGNOSIS.

The diagnosis of acute subdural abscess should not be unduly difficult if one is familiar with the usual course followed by this condition and realizes the possibility of its existence in the case at hand. Failure to make this diagnosis is most frequently due to failure to consider the possibility of this serious complication. In acute suppurative frontal sinusitis, with or without antecedent sinus disease, followed by orbital swelling, persistent headache, malaise, fever, at times with chills, meningeal signs and lethargy, one should be very suspicious of subdural abscess. Under such circum-

stances, should evidences of profound intracranial disease suddenly appear, the diagnosis is almost certain. Courville[2] stated as a "clinicopathologic aphorism" that "in the presence of acute frontal sinusitis (empyema) the sudden onset of Jacksonian convulsions, hemiplegia and (if the major side of the brain is affected) aphasia, usually indicate the development of a subdural abscess." Jacksonian attacks occurred in three of our cases, and the intracranial complication was heralded by a generalized seizure in Case 4. It is important not only to diagnose the presence of subdural abscess but also to determine its location; this is frequently possible by clinical evidence alone. Collections of exudate over the frontoparietal convexity and Sylvian fissure cause focal convulsive attacks involving the eyes, face and upper extremity. Usually this is soon followed by a weakness of the face and upper extremity, and dysphagia (in leftsided lesions). As the hemiparesis increases, there is usually paralysis of conjugate gaze to the paretic side; however, in stuporous individuals this sign may not be elicited. On the other hand, collections of pus in the longitudinal fissure are apt to produce Jacksonian attacks affecting the leg, followed by a paresis and sensory loss in the lower extremities with progressive weakness of the entire side, usually sparing the facial muscles.

Although the abscess will usually be found on the side of the known frontal sinusitis, it should be appreciated that the circumstances may lead to the development of an abscess on the opposite side. This is readily understandable when one realizes that a frontal sinus may extend across the midline, thus having its posterior wall in apposition to the dura on both sides of the sagittal sinus; moreover, closure of the septum between the frontal sinuses is frequently incomplete, and both frontal sinuses are diseased, though the symptoms may point largely to one. Bilateral suppurative frontal sinusitis was present in all four of our cases. It must be remembered that if the subdural abscess develops by an extension of thrombophlebitis through the sagittal sinus, it is a matter of chance on which side the space becomes infected, and in fact, bilateral disease may develop. Occasionally the paralysis may develop on the same side as the lesion and,

when this does occur, it is thought to be due to marked displacement of the brain, causing pressure of the edge of the tentorium against the peduncle of the opposite cerebral hemisphere. Dilatation of the pupil, when present, is a good lateralizing sign, but even this sign is not infallible. Pupillary inequality was not noted in any of our patients.

The optic fundi do not usually show papilledema; however, engorgement of the veins is usually present, and in neglected cases, early low-grade papilledema may be found. One of our cases showed beginning papilledema.

The temperature is usually moderately elevated and the pulse somewhat slower than one might expect for the degree of fever. The white blood cell counts ranged from 19 to 31,000 in our cases, and there was a predominance of polymorphonuclear cells (see Table II).

The cerebrospinal fluid pressure is elevated, ranging between 190 to 460 mm. of fluid in the late stages of the disease. The fluid is usually slightly turbid due to a pleocytosis of from a hundred to several thousand, with a predominance of polymorphonuclear leucocytes. Only in one instance were we able to grow organisms on culture from the spinal fluid (see Case 4). This indicated a concomitant septic leptomeningitis. Roentgenograms of the skull and sinuses usually depict nothing more than clouding of the sinuses. It is common knowledge that Roentgenographic changes in bones do not appear for about a week after infection has set in, and, therefore, Roentgenograms cannot be depended upon in the diagnosis of subdural abscess. Should sufficient calcium be present in the pineal body for Roentgenographic visualization, a lateral shift of the pineal would become a significant lateralizing sign.

Differential diagnosis of acute subdural abscess lies between intracerebral abscess, epidural abscess, purulent meningitis and longitudinal sinus thrombosis. Extradural abscess gives rise to a much milder illness than does subdural abscess. Usually there are only mild signs of meningeal irritation, no focal signs of cerebral damage, and the patient does not

appear critically ill and does not run a drastic fulminating course. In the patient with increasing intracranial pressure, meningeal signs, stupor, focal neurologic signs or symptoms, the discovery of extradural pus should not lead one to believe this to be the only complication; subdural abscess may very likely be present in addition to the extradural abscess; such were the findings in Case 4 of our series.

Purulent meningitis, when accompanied by thrombosis of cortical veins, may often confuse the diagnosis, although this condition is rarely a sequela of frontal sinusitis. The course of meningitis, as a rule, is not as drastic as subdural abscess; progressive focal neurologic signs are not usually present, and the cerebrospinal fluid pleocytosis is usually much higher than that in subdural abscess. The presence of meningitis in a patient with focal neurologic signs does not detract from the diagnosis of subdural abscess. In fact, the two may coexist (see Case 4).

The invasive stage of intracerebral abscess formation is milder, less dramatic and more protracted than subdural abscess. The headache is less severe and varies considerably in intensity. The temperature does not reach excessive heights and subsides after a short time. Meningeal signs are usually absent and pleocytosis is much less marked. Intracerebral abscess may form rapidly at times, simulating a true cerebritis, and create a clinical picture indistinguishable from subdural abscess. In such instances, an immediate trephination in the frontal region under local anesthesia will settle the issue without jeopardizing the patient.

Thrombosis of the longitudinal sinus may simulate a syndrome of subdural abscess, and in fact, the two may be coexistent. In thrombosis the course is variable and the temperature curve septic in type. Alternating convulsions, right and left, are often present, beginning in the foot, and bilateral neurologic signs are usually found in both lower extremities. Meningeal signs are mild or absent in longitudinal sinus thrombosis, and the cerebrospinal fluid shows little or no pleocytosis.

PREVENTION.

Subdural abscess is prevented from developing in most cases of frontal sinusitis by active treatment of the sinus, including drainage, when indicated, and the administration of sulfonamides and antibiotics. It is the responsibility of the rhinologist to determine when operative intervention for frontal sinusitis is indicated. Such decisions should be made with full knowledge of the fact that chemotherapy and antibiotics are not a substitute for sound surgical principles but are adjuncts which may even extend the field of surgery. If this dreadful complication of suppurative frontal sinusitis is to be prevented, we must be on the alert for signs of failure of conservative measures and antibiotics. The appearance of the posterior bony plate at the time of sinusotomy cannot be relied upon in determining whether or not the infection has spread intracranially. In our cases necrosis of the posterior plate was found in only one instance (see Case 4); therefore, if the surgeon does not feel that the posterior bony plate should be opened at the time of providing open drainage of the sinus, he should be on the alert for warning signs which are usually present for days before the development of a subdural abscess. The dura in the region behind the frontal sinus is pain sensitive, and the reference of the pain is in the local frontal region. Inflammation of the dura or pressure of a local extradural abscess is sufficient to incite pain. The persistence or the development of frontal headache after simple frontal sinusotomy is very suggestive of the presence of extradural infection. There may be accompanying low-grade fever, leucocytosis, and, in the later stages, lethargy and signs of meningeal irritation. An extradural abscess can be relieved only by drainage, and if allowed to persist will certainly lead to a subdural abscess or other serious intracranial infection. This is clearly demonstrated in Case 4; therefore, the persistence or the recurrence of frontal pain with or without other signs should be an indication for opening the posterior wall of the frontal sinus.

The rhinologist should not be deterred from removing the posterior wall of the frontal sinus, when indicated, by the

fear of leaving the patient with a marked deformity of the forehead. These bony defects may be repaired at a later date, when the infection has subsided, by appropriate cranioplasty without any difficulty. We have carried out cranioplasty on Cases 1 and 2 and repaired the bony defect with a tantalum plate. By use of a coronal incision, cranioplasty has been carried out without a visible scar outside of the hair line (see Figs. 1 and 3). Case 3 is to report for tantalum plate cranioplasty in the near future.

TREATMENT.

Acute subdural abscess must be regarded as an emergency, and immediate operative intervention is mandatory. Simple trephination of the skull in the frontal region will immediately establish the diagnosis. Both sides should be explored so that bilateral involvement may not be overlooked. Failure to explore both sides at the time of recurrence of difficulty in our Case 4 resulted in a fatality because of an overlooked collection over the convexity of the unexposed right hemisphere which did not produce localizing signs. Measures to control the infection should be taken promptly, and, before surgery is attempted, antibiotics and sulfonamides should be given in massive doses. Time should not be wasted in awaiting the outcome of the bacteriological studies to identify the responsible organisms whereby the appropriate drug can more accurately be selected. One to two hundred thousand units of penicillin should be administered intramuscularly every three hours. Sodium sulfadiazine in a dosage of 4 gm. should be given intramuscularly immediately and should be administered in appropriate divided doses in the amount of 6 gm. per 24 hours. Once these measures have been instituted in an effort to inhibit the spread of infection, immediate drainage of the pus from the subdural space of these extremely ill patients is mandatory. In the early stage of this disease the pus is liquid and easily drained; however, in the chronic state the pus is transformed into a thick plastic exudate. Moreover, the early drainage of the exudate from the subdural space, while it is confined to the frontal pole and before

it has extended posteriorly over the sensorimotor cortex of the brain, may lessen the incidence of the dreaded sequela, convulsive disorders.

The primary incision for the identification and drainage of an acute subdural abscess should be made over the suspected site of the lesion, in a clean field, in the midfrontal region. If pus is found, the burr hole is enlarged slightly and additional openings are made in the parietal, temporal and even the occipital area until the full extent of the collection has been defined. Once the extent of the exudate has been established, the pus is aspirated from the subdural space, and the space is carefully and gently washed out with warm saline. In extensive collections, multiple burr holes are necessary. Through these openings through-and-through irrigation may be facilitated. In the face of intracranial hypertension, the subdural space may be more easily drained and irrigated after collapsing the cerebral hemisphere by removing 25 or 30 cc. of fluid from the lumbar thecal sac, as suggested by Kahn.[10] After the pus has been thoroughly removed and subsequent irrigation fluid returns clear from all directions over the hemisphere, a small soft rubber catheter is introduced into the subdural space through each burr hole.

If interhemispheral subdural suppuration is suspected or found, cranial openings should be made as near to the midline as possible. Keith and McKenzie[7] have advocated removal of a long narrow paramedian strip of bone for effective drainage of the sagittal fissure. This was carried out in Case 4 of our series at a secondary operation. More recently, List[8] has accomplished drainage of the longitudinal fissure by means of multiple burr holes in the parasagittal region, in the frontal, parietal and occipital areas.

Although there was very little drainage through the inlying catheters, they served as a means of injecting penicillin into the subdural space in two of our four cases. Penicillin in concentration of 1,000 units per cc. was used. In Case 2, 15,000 units were injected daily for two days, and 10,000 units daily for five days. In Case 3, 10,000 units were left

in at the time of operation, and 10,000 units were instilled daily for four days, and 5,000 units on the three succeeding days. Case 1, treated in 1946, prior to the publishing of the works of Schiller, Cairns and Russell,[6] did not receive subdural instillation of penicillin. Case 4, our most recent patient, likewise was not treated with instillation of penicillin in the subdural space. This patient made an apparently good recovery from a left subdural abscess; however, he succumbed to a collection of pus over the opposite hemisphere which had spread from the orbital surface of the left frontal lobe to the longitudinal fissure beneath the falx and over the right hemisphere. Both of the patients who had no penicillin instilled into the subdural space had convulsions previous to drainage; however, only one had convulsions in the immediate postoperative period and then for only two days. The remaining two patients who had instillation of subdural penicillin, both had preoperative and postoperative convulsions, the postoperative convulsions being troublesome for three days in one and five days in the other. Although the number of cases involved is too small to draw any conclusions, in view of the fact that concentrated penicillin solution in contact with the cerebral cortex in itself may produce convulsions, one wonders whether or not this procedure is either necessary or justifiable. It is not beyond the realm of possibility that intramuscular penicillin in sufficient dosages and adequate sulfonamide therapy would prove sufficient to prevent the spread of the infection. This question is certainly deserving of further consideration. Schiller, Cairns and Russell[6] have advocated injecting large quantities of penicillin solution containing 500 units of penicillin per cc. into the subdural space every three hours for several days. Gurdjian and Webster,[5] and List[8] recommend the instillation of about 30 to 50,000 units of penicillin in a smaller volume of fluid three times daily.

The details of the dosage and duration of systemic administration of antibiotics and sulfonamides in our cases are depicted in Table VI. Careful attention to the general care is highly essential, inasmuch as these patients are critically ill and in need of competent nursing, adequate diet, blood transfusions and general supportive measures.

The importance of removal of the original focus of infection, if possible at the same time as the surgical management of the intracranial complication, cannot be too strongly emphasized. Empyema of the frontal sinuses and osteomyelitis of the frontal bone should be eradicated. In two of our four cases the subdural abscess was drained and bilateral frontal sinusectomy with resection of an additional portion of the frontal bone was accomplished in one sitting. In one instance left frontal sinusectomy with exposure of the dura was carried out 22 hours previous to drainage of the subdural abscess; in this particular instance the diagnosis was not entirely clear previous to sinus operation, and the possibility of an epidural abscess was held to be most likely. In one case previous frontal sinus surgery, which had been too conservative, was done sometime prior to the drainage of the subdural suppuration; this patient was later subjected to complete eradication of his frontal sinuses in his convalescent period.

SEQUELAE.

Three of the four patients in this series survived. The follow-up periods are five years, two years and one year, respectively. The three living patients are all gainfully employed, and their position and station in life have not been materially altered. The most undesirable sequela among these patients thus far has been convulsive seizures; all had convulsions prior to their operative treatment. All three survivors had Jacksonian seizures in the immediate postoperative period. Case 1, who has now been followed for five years, is well controlled with anticonvulsant therapy and has had no seizures in 10 months. Case 2 has had no generalized seizures since institution of anticonvulsant therapy and occasionally has a mild Jacksonian seizure implicating the right face, lasting a few minutes at a time, at a frequency of once a month. Case 3 is well controlled with anticonvulsant drugs and has an occasional mild Jacksonian seizure implicating the right face and arm, lasting a few minutes at a time, and recurring no more frequently than every two months. The frequency of a residual convulsive state is understandable in view of the cortical cicatrization which takes place secondary to the inflam-

matory reaction. In the future it may be of interest to clarify the rôle of the instillation of penicillin into the subdural space in producing an increased frequency of convulsions. On the other hand, earlier diagnosis allowing surgical intervention, when the pus is limited to the frontal pole, perhaps offers the best chance of preventing this undesirable sequela.

SUMMARY AND CONCLUSIONS.

Acute subdural abscess is a serious, though infrequent, complication of suppurative frontal sinusitis which constitutes a distinct clinical and pathological entity, the diagnosis of which is not difficult if one is cognizant of the possibility.

The diagnosis, pathogenesis and treatment of the condition is reviewed, and our experience with four cases is reported. The sudden onset of Jacksonian convulsions and focal neurologic signs in the presence of acute suppurative frontal sinusitis usually indicate the presence of a subdural abscess. The abscess may be a fulminating and rapidly fatal infection. It is usually limited in the beginning to one side, but, if undrained, tends to spread over the entire cerebral hemisphere and, in the late stages, to the opposite side. Early diagnosis and treatment are necessary for a successful result. Treatment consists of massive administration of antibiotics and sulfonamides with immediate evacuation of the purulent collection through strategically placed burr openings and instillation of penicillin into the subdural cavity. The importance of bilateral exploration is stressed. Unfortunately, convulsive seizures are all too often a serious sequela.

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Doctors' Building, Kings Drive.

THE PRESENT STATUS OF GLOBUS HYSTERICUS.*

RALPH G. RIGBY, M.D.,
Salt Lake City, Utah.

It is my opinion that so-called "globus hystericus" has played a very important part in our practice in the field of otolaryngology and bronchoesophagology, and that too little time has been spent in the diagnosis and treatment of these patients. It is agreed that the difficulty in differentiating between functional disturbances and organic disease at the level of the upper esophagus has contributed to this apparent state of confusion. The lack of interest manifested by physicians, in diseases in the upper end of the esophagus, pharynx and larynx, and their tendency to ascribe symptoms of an indefinite character to functional or emotional disturbances, has been an added factor in stimulating my investigation of the subject.

It is believed by most authors that the symptom complex of "globus hystericus" is based upon certain mental stigmata in which the chief clinical symptoms are headaches, often severe; some pains, which are centered in the small of the back; spells of laughing and crying which are uncontrollable; poor sleeping habits with terrible dreams; irregular movements of the body, kicking of the legs; throwing the head from side to side; rolling on the bed; and a feeling of "fullness" or "choking" in the throat, which leads to the term of "globus hystericus." Patients do not, however, go into coma, nor do they exhibit any convulsions.

Much was written in the early days about the special types of "psychoneurosis"; and some of the authors emphasized the disorders of the muscles and the muscle fibres, especially in their relationship to the complex chemistry of the muscle

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itself, particularly in its relationship to creatine and creatinine metabolism. If some of the later writings upon this subject are to be considered important, and if we are to consider muscle spasm as part of this phenomena, then it must be understood that the *disorders* of the muscle must be taken into consideration.

Another phase of the subject which is very interesting is the clinical facts about the "hysteria" reported by various authors. It is considered that there are three forms of hysteria: primary, secondary and tertiary, according to whether the manifestations are associated directly with an uncontrolled emotional tone, a discomfort of any description, or with the expectation of discomfort, respectively.

"Globus hystericus" is most likely classified as *a.* regressive and *b.* secondary, and the symptoms arise in an atmosphere associated with discomfort in the broadest sense of the word and in any part of the body.

It was thought in the beginning that this condition was more common in the female, particularly after puberty, and that hysteria itself reacted with abnormal ego contricity — an ego that demanded attention. The hysterical patient wants to be noticed without interference of his personal habits. An outstanding feature of an hysterical patient is his apparent emotional placidity and general air of detachment from his surroundings. He is interested in his symptoms, but his interest is rather that of an onlooker than a participant. He is invariably courteous, but is never anxious or disturbed.

Now, as you can see from the foregoing resumé, there are certain stigmata to which we attach the term "globus hystericus." There seems to be a realm of facts to support the idea that a true functional "globus hystericus" does exist; however, in mild cases these patients are satisfactorily treated by either the general practitioner or the internist who sees them first, and the majority are not referred to the endoscopist or the otolaryngologist (speaking personally, it is a rare happening that a case with marked functional "globus hystericus" is referred to me for treatment); therefore, the

diagnosis which has been established by the aforementioned information can be properly treated only by one specializing in psychiatry or nervous disorders.

It is my experience that organic disease produces a symptom complex which can be referred to as "globus hystericus." Here I am referring to patients under my own supervision who complain of a "lump in the throat" as their most outstanding symptom — and the phrase is usually forced upon the patient by the physician because the patient himself is unable to describe the vague sensation which he feels. This single complaint has been found to occur in primary infections of the pharynx or upper esophagus. It has also occurred in patients with diabetes; rectal polyps; G. I. upsets due to dietetic errors; diseases of the thyroid gland; elongated uvula; telangiectatic tumors of the vocal cords; allergies; trench-mouth of the gums; tuberculosis; thyroglossal-duct cysts; lingual goiter; long styloid process; ossifications of the ligaments; carcinoma of the larynx, pharynx and upper esophagus; and eye strain corrected by glasses. In every case this single symptom has disappeared after adequate treatment of the organic disease. It, therefore, appears that many cases diagnosed as "globus hystericus" with the sole complaint of a "lump in the throat" and without any of the other associated stigmata of "hystericus" respond to treatment of their organic disease. Can such cases then be classified with those in the realm of "functional disorders?"

It is now that I wish to discuss my own experience with the patients who have been referred to me by other physicians because these patients have a "lump in their throat." These people are put well at ease before the examination begins, and a careful history is obtained regarding the present illness and all factors in the past history of the patient which should have a bearing on the outcome of the interview. It is true that in many of these cases there have never been any other stigmata of disease except the one symptom of a "lump in the throat." The patient is very carefully interrogated regarding his emotional disturbances, such as hostility, anger, rage, resentment, fear and jealousies. Other possible

emotional factors are domestic troubles, sexual difficulties or frustration, forms of guilt, financial worries, frustrated ambitions, discouragement for any reason, fright or worry. These suspicions must be removed as a causative factor in the patient's "symptom" before an inquiry is made regarding the nutrition of the patient, whether or not they have easy fatigue or exhaustion, whether some accident or trauma has had to do with their present illness, etc. Although I am sure that my approach to the problem is not so good as that which could be performed by many general practitioners, internists or psychiatrists, I believe that in many of these cases I have been successful in obtaining enough insight into the patient's emotional stability to form an opinion as to whether the patient should be treated as a very mild type of hysterical individual, or whether, if my findings should disclose organic disease, he could be treated without being referred for special psychiatric therapy.

There has been another interesting problem which has confronted me regarding these patients. I have to report on 98 individuals who have come to me with the symptom of a "lump in the throat." Most of these have been diagnosed as a mild type of "hysteria." The others have been found to have organic disease which has been treated adequately following diagnosis. The large group has had X-ray examinations of the neck, which revealed two characteristic phenomena: one they have marked hypertrophy of the lingual tonsil, which is very easily seen by indirect examination of the pharynx, and which is confirmed by the lateral X-ray films of the neck; second, they have marked lipping or osteoarthropathy of the anterior borders of the cervical vertebra.

At this point I would like to refer to my investigation into this subject and in a small way attempt to show that *marked lipping of the cervical vertebra with the so-called inflammatory reaction in the soft tissues anterior to the lipping may be the causative factor in setting off the trigger mechanism which produces the "symptom."* I have several slides which have been prepared from this large series of nonorganic cases.

The few shown here are characteristic of the anterior lipping, and in my opinion produce a serious problem in the diagnosis and treatment of "globus hystericus."

* * * *

To me this seems to be as logical an explanation as hyperirritability of the mucous membrane, spasm of the cricopharyngeus muscle, irritability caused by enlarged lymph nodes, etc.

My success in treating these patients has been due to the fact that I have been able to establish a true emotional relationship between the patient and myself, so that this lonely symptom of a "lump in the throat" which the patient originally complained about has disappeared.

I believe that we are duty bound as physicians, and particularly as otolaryngologists, to examine these patients thoroughly and treat them according to their needs, which, of course, are determined by careful and complete physical examination.

CONCLUSION.

"Globus hystericus" or a "lump in the throat" can be a symptom of functional disorder, either mild or severe, or of organic disease. The diagnosis is based upon a complete history and physical examination. Psychiatric treatment by the physician who is willing to establish a true emotional relationship between the patient and himself. Organic diseases should be treated as such. A new observation has been discussed and I trust that this brief review of the past will stimulate more activity on this subject in the future.

BACTERIOLOGIC AID IN RHINOLOGIC DIAGNOSIS AND TREATMENT: IMPROVED CRITERIA.*†

JOSEPH L. GOLDMAN, M.D.,
New York, N. Y.

The progress of medicine has run a parallel course with the development of improved methods of diagnosis and treatment. The basic sciences especially have contributed much to the origin of newer concepts of disease processes. It is the purpose of this communication to show how bacteriologic investigations, done in a simple manner, suitable for office procedure, can improve greatly the understanding of nasal and sinus disease and the indication for therapy.

As in other fields, the old standard methods of physical diagnosis in rhinology very often fail to provide the definitive information which is required to establish accurate diagnosis. Direct examination of the nose and nasopharynx and transillumination and Roentgen examination of the paranasal sinuses frequently do not reveal the findings needed for a correct evaluation of rhinologic problems.

During the past several decades, lavage of the large sinuses has been accepted as a valuable additional diagnostic method. Frequent use of this procedure for diagnosis has demonstrated that secretion can be washed out of a maxillary antrum or sphenoid sinus, for instance, even though transillumination and X-rays have shown the sinus to be clear. The Roentgen examination has more reliability than transillumination, but both these methods can fail to detect the existence of secretion.

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†From the Otolaryngological Service, the Mount Sinai Hospital, and Department of Otolaryngology, New York University Postgraduate Medical School.

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One of the significant manifestations in nasal or sinus disease is a discharge of fluid material or secretion. This material, as we all know, may vary considerably in consistency, color and amount. It has been my experience to find many micro-organisms in small amounts of mucoid secretion irrigated from sinuses and, on the other hand, no micro-organisms or cellular evidence of infection in large amounts of secretion obtained from sinus lavages; also, I have found the consistency or color of the secretion to be no index of infection, thus, the amount and appearance of nasal and sinus secretion *per se* may not predicate infection or indicate degree or kind of infection.

It is true that an obviously purulent infection can be recognized often by direct examination, but such a case rarely presents a problem in diagnosis. It is the instance in which the presence of a discharge is mistaken for infected secretion that may lead to erroneous diagnosis and treatment. The designation of mucus or pus should be reserved for characterization only after microscopic examination and culture of the secretion have been made. The term "secretion" is used arbitrarily in this discussion to describe nasal and sinus discharge.

One of the reasons for errors in rhinologic diagnosis has been that in the past the term "infection" has been used loosely and applied inaccurately in the evaluation of various rhinological disturbances. To prove the existence of infection, it is not only essential to demonstrate the presence of micro-organisms but also their active multiplication. Parenthetically, it should also be stated that infections always begin on the surface of the mucus membrane, and if uncontrolled, then the bacteria invade the deeper tissues.

In order to emphasize this concept, may I remind you of the simple admonition given to students of clinical microscopy, that a cloudy urine doesn't necessarily imply the presence of white blood cells or infection. A diagnosis of infectious or bacterial meningitis, for instance, is also made only if a micro-organism is isolated and cytologic and chemical changes occur in the fluid.

The problem most commonly encountered in rhinologic diagnosis is the differentiation of infections from noninfectious disorders of the nose and sinuses. Many of these noninfectious conditions belong to the broad category of vasomotor rhinitis. Allergic rhinitis comprises a significant entity in this category. Skin and other kinds of testing for pollen and other types of sensitizing agents has proved valuable in distinguishing allergic rhinitis from other diseases of the nose and sinuses. It is now being recognized that in a large number of patients suffering from vasomotor rhinitis, the etiologic factors may be physical, psychological or constitutional. The use of local medicaments may also be responsible for vasomotor reactions.

Bacteriologic and cytologic examinations of secretion obtained from the nasal cavities and paranasal sinuses are usually valuable and frequently necessary to establish clearly the presence of an infectious or vasomotor disturbance. They should be regarded as principal diagnostic procedures. It should be realized that the accuracy of such diagnostic criteria cannot be expected to be greater than any ordinary laboratory procedure; however, it has been my experience that this approach to the diagnosis of rhinologic disease has proved to be much more helpful than the standard method of physical examination alone.

It may be stated that routine cultures of nasal and sinus secretions together with microscopic examinations of these secretions provide: *1.* a precise diagnostic method to differentiate specific infections and vasomotor rhinitis; *2.* a rational basis for the use of specific antibiotic and chemical therapy; and *3.* consequently, improved diagnostic criteria for nasal and sinus disease.

The technique for the bacteriologic and microscopic study of nasal and sinus secretions which has been found to be most effective in office or routine hospital practice has been as follows: A sterile platinum loop is applied to the reactive mucous membrane in the sphenoethmoidal recess, the middle meatus and over the turbinates for the removal of secretion.

If the discharge is copious, a sterile capillary pipette is used for this purpose. It is believed that the platinum loop is far superior to a cotton applicator, which is liable to cause gagging and contamination from nasopharyngeal secretion. When a nasopharyngeal culture is desired, a curved large loop is carefully passed through the mouth into the nasopharynx, avoiding contamination. Secretion from a sinus is collected in a basin under "surgically clean" conditions and is aspirated into a sterile capillary pipette for bacteriologic study.

Secretions are spread on clean glass slides for microscopic study and are stained with Wright stain for routine purposes. Such spreads permit microscopic identification of micro-organisms, when present, and cellular elements. If desired, the Gram stain should be made to differentiate the Gram positive and negative micro-organisms. The Hansel stain is of value for the clearer delineation of the eosinophile.

All cultures are made routinely on blood agar plates alone. Not only are micro-organisms easily grown on blood agar but the opportunity for quantitative estimation, which is so important, is also afforded by this method.

The data which should be obtained in the microscopic examination of nasal and sinus secretion is the following: *1.* the number and kinds of micro-organisms; *2.* the amount of mucus; and *3.* the types of cells. In infections, as a rule, in contradistinction to vasomotor disturbances, bacteria can be found readily on spreads and can be correlated usually with a pathogenic micro-organism on culture. Neutrophilic polymorphonuclear cells are also commonly found in large numbers. Mucus is a prominent finding in allergic and vasomotor rhinitis, while it tends to be lacking in infections. The belief is that active growth of bacteria destroys mucus. Although allergic and vasomotor rhinitis may exist without eosinophiles appearing in the nasal secretion, their presence in moderate and in especially large numbers strongly suggests such a diagnosis, particularly if no micro-organisms are seen in the spread. It should be mentioned that a severe eosinophilic rhinitis can produce secretion with purulent characteristics.

The information which should be sought in the culture is whether the micro-organism which has been obtained from the nose or sinus is pathogenic or nonpathogenic and the quantitative estimation of such micro-organisms. Inasmuch as pneumococci, hemolytic streptococci, hemophilus influenzae and parainfluenzae and Klebsiella pneumoniae are found very rarely in the normal nose or sinus, even in very small numbers, isolation of any of these micro-organisms from the secretion in the nasal cavity or irrigated from a sinus strongly suggests the presence of infection. Moderate or large growth on culture of staphylococcus aureus A, streptococcus viridans, streptococcus nonhemolyticus, proteus bacillus, pseudomonas aeruginosa also suggests the existence of infection, particularly if found on repeated occasions. The probability of infection is further substantiated if in addition spreads of stained secretion show similar micro-organisms and neutrophiles. It should be mentioned that these micro-organisms can be isolated from nasopharynges which show no evidence of infection. In other words, these potentially pathogenic micro-organisms are present in the normal nasopharynx. It is my belief that the nasopharynx is the carrier-focus of pathogenic micro-organisms which spread into the nose (and also into the tracheobronchial tree) and cause infections when the antibacterial barriers are broken by lowered resistance of the nasal mucosa.

On the other hand, staphylococcus albus, staphylococcus aureus B, diphtheroids, Neisseria pharynges and staphylococcus aureus A in very small numbers are present in the normal nose and as a rule are not associated with infection; thus, if any of these micro-organisms, alone or in combination, are cultured from nasal or sinus secretion, it is unlikely that infection exists. If spreads of such secretion show no micro-organisms, or just a few, and a large amount of mucus, then the evidence is strong that one is dealing with a vasomotor disorder.[1]

The causative agent of a sinus infection occasionally can be a micro-organism which is usually nonpathogenic. For instance, I have recently treated an acute frontal sinusitis due

to proteus vulgaris. Before such a micro-organism is accepted as the cause of the infection, it should be repeatedly isolated and be identified by microscopic examination of a spread of the secretion. In the patient mentioned, the Gram negative bacilli were present in large numbers in the direct smear.

A sinus infection, the secretion of which shows Gram positive cocci on spreads but fails to grow any colonies on repeated cultures, should suggest the possibility of an anaerobic micro-organism, such as anaerobic streptococcus hemolyticus. I have observed an anaerobic streptococcal infection of a maxillary antrum associated with erythema nodosum. These lesions disappeared, the sedimentation rate and the temperature, which had been elevated, returned to normal and systemic manifestations of the illness subsided with the cure of the sinus infection.

Thus, correlation of the kind and number of micro-organisms found on examination of nasal spreads with those of cultures made from the same secretion can provide pertinent and significant information as to the nature of the rhinologic status. The interpretaton of the bacteriologic and cytologic findings of the nose and sinuses in health and disease is outlined in the following table:

TABLE 1.
INTERPRETATION OF BACTERIOLOGIC AND CYTOLOGIC FINDINGS.

	Bacteriology	Cytology
Normal Nose	Nonpathogens 0 to 2+ colonies	No or few micro-organisms Mucus 0 to 1+ Polys. 0 to 1+
Vasomotor (Allergic) Rhinitis and Sinusitis	Nonpathogens 0 to 2+ colonies	No or few micro-organisms Mucus 3 to 4+ Usually eosins. to 4+ Occas. polys alone
Nasal and Sinus Infections	Pathogens 1 to 4+ colonies	Micro-organisms often 3 to 4+ Mucus 0 to 2+ Polys. to 4+
Vasomotor (Allergic) Rhinitis with Infection	Pathogens 1 to 4+ colonies	Micro-organisms often 3 to 4+ Mucus 3 to 4+ Usually eosins. to 4+ Polys. to 4+

1+ = Small 2+ = Small to Moderate 3+ = Moderate 4+ = Large

In view of the number of antibiotics available and new antibiotics constantly appearing, bacteriologic investigations with susceptibility tests on a routine basis permit the proper utilization of specific antibiotic and chemical therapy. This principle is generally accepted in theory but not in practice. Although hemolytic streptococci and pneumococci, as a rule, are susceptible to the antibiotics, the staphylococci and the Gram negative bacilli which are found in upper respiratory infections may show considerable variations in susceptibility. There is evidence that even the pneumococcus may be occasionally resistant to penicillin.[2] Now that dried antibiotic discs are available for such testing, preliminary or approximate information concerning the susceptibility of a microorganism can be obtained with simple facilities and in a short time.[3-5] The serial dilution method of testing offers, of course, greater accuracy and should be carried out whenever possible. I can recall, for example, a number of staphyloccus aureus A sinus infections which were resistant to penicillin but sensitive to aureomycin, an acute frontal sinusitis due to hemophilus influenzae which responded to therapy after the administration of sulfadiazine and streptomycin, and the acute frontal sinusitis caused by proteus vulgaris mentioned above, which reacted favorably to chloromycetin but not to aureomycin.

Precision in diagnosis of nasal and sinus infections is also necessary to restore the problem of foci of infection of these areas on an acceptable basis. In the past few decades, the relationship of foci of infection of the paranasal sinuses to systemic diseases has been in a state of confusion. The main reason for this, in my opinion, has been the incomplete and inadequate information as to the actual presence or absence of infection. Thorough correlation of bacteriologic and cytologic examinations along the lines indicated will greatly help to clarify the relationship that does exist between nasal and sinus infections and systemic diseases.

SUMMARY.

It is suggested that bacteriologic and microscopic study of nasal and sinus secretion should be used as major criteria in

the determination of nasal and sinus disease. A correlation of these two investigative procedures leads to a more precise diagnostic evaluation. This method can be very helpful in differentiating the infectious from the noninfectious diseases of the nose and sinuses. Susceptibility tests with antibiotic discs on isolated micro-organisms provide a rapid means to determine specific antibiotic and chemical therapy.

1050 Park Avenue.

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BLEEDING FOLLOWING TONSILLECTOMY.*†

SAMUEL L. FOX, M.D.,
Baltimore, Md.

Tonsillectomy is the most frequent operation in modern surgery. In spite of the many advances made in anesthesia, in fluid and electrolyte physiology, and in surgical technique, the one great unconquered hazard of tonsillectomy is bleeding.

An analysis of the cases of bleeding following tonsillectomy reveals two periods of high incidence of such bleeding: a period immediately following surgery, and a period usually five to eight days later. This permits classification of such bleeding as *a.* primary bleeding, and *b.* secondary (late) bleeding. The causes and management of these two types of bleeding are different and unrelated.

PRIMARY BLEEDING.

Primary bleeding occurs within the first 24 to 48 hours postoperatively but may persist throughout the period of convalescence unless checked. In the majority of instances, primary bleeding is due to inadequate surgical hemostasis at the time of operation; to the loss of a ligature from the throat during the reaction period or soon thereafter, or to some constitutional disorder which interferes with the proper clotting of blood. The first two causes are almost always due to faulty surgical technique, and the last named may be obviated by a proper preoperative history and laboratory examination of the patient. In the author's experience, primary bleeding is at least as common from the adenoid fossa as from the tonsillar fossae, whereas secondary (late) bleeding is preponderantly from the tonsillar fossae.

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†From the Department of Otolaryngology of the University of Maryland School of Medicine.

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SECONDARY BLEEDING.

Secondary bleeding occurs from two to 10 days postoperatively, with the highest incidence on the fifth and sixth days. Predisposing factors and direct causes for secondary (late) hemorrhage include acute febrile diseases occurring during convalescence; dietary deficiencies, particularly vitamins and proteins; hypertension; local infection; local trauma; blood dyscrasias; and certain drugs, notably aspirin, administered either locally or systemically during the convalescence.

In tonsillectomy and adenoidectomy, sizeable areas are left raw and uncovered, and healing by secondary intention must take place. Superficial infection by invasion of the bacterial flora of the mouth and throat is the rule. The reaction to bacterial invasion, plus the normal hemorrhagic and serous exudation which occur on such a raw surface, produces a crust which finally covers the entire surface of the wounds. If this crust remained undisturbed, the problem of secondary bleeding would be minimized; however, the crust is continually under stress and strain by the normal movement of the regional muscles. Granulation tissue promptly begins to form beneath the crust, growing from below upward, and results in displacement of the crust in from seven to 10 days. As the crust slowly disintegrates or becomes dislodged, the granulation tissue is often exposed, and hemorrhage may result. As mucous membrane proliferates to cover this granulating surface, the possibility of bleeding from dislodgment of the crust is reduced accordingly.

Attempts to produce *per primum* healing by sewing together the pillars, or by suturing the superior plica across the fossa, have all come to naught. The sutures are soon torn out by the movements of the pharyngeal muscles, and during the interim the patient suffers severe pain on attempted swallowing or talking.

It is obvious that every attempt should be made to control acute febrile diseases, local infection, hypertension and blood dyscrasias, and to avoid local trauma during the convalescence. The patient must be impressed with the importance of

obtaining all necessary elements of diet, and of avoiding any harmful drugs or measures during the convalescence. The need for an adequate protein intake during the postoperative period cannot be overemphasized.[11] For this purpose the author provides the patient or parent with detailed printed instructions immediately following the operation (see Fig. 1).

FIGURE 1.

DR. SAMUEL L. FOX

1205, St. Paul St., Baltimore 2, Md.

INSTRUCTIONS FOR CARE AFTER TONSILLECTOMY

For.....

1. The patient should remain in bed for the first two days after operation. On the third day he may be up but must be quiet. On the fourth day he may go outdoors if the weather is good but he may not run, play or exert himself (bending, stooping, lifting, swimming, etc.) for at least seven days. On the eighth day he may return to school or to light work.
2. A daily bowel movement is important. Two to four teaspoonfuls of Phospho-Soda (Fleet) in half glass of water on fasting stomach is recommended. If results are not prompt, an enema may be administered.
3. If the throat feels dry, or the breath is foul, the patient may gargle 4 or 5 times a day with a solution made by dissolving ¼ teaspoonful of table salt in a full 8 ounce tumbler of lukewarm water. *No other gargles may be used.* Children do not use gargles well. DO NOT USE "ASPERGUM."
4. Abundant fluids and an adequate diet are absolutely essential for a speedy recovery. The patient must take fluids immediately after operation and he must begin to take food the next day, as otherwise troublesome muscle spasm will result and swallowing will become very painful. If this happens, the patient must be encouraged to take food in order to overcome the spasm.
5. Frequent small meals are preferable to a few large ones. No hot drinks or food should be taken; all foods and drinks should be cold or lukewarm. The diet should consist of:

   1st day after operation: Take abundant quantities of water, milk, ginger ale, Coca-Cola, warm or cool broth, ice cream or sherbet, eggnog, and prune juice. Orange and grapefruit juice are not well tolerated unless sweetened. These are best taken cold and in small quantities frequently repeated.

   2nd day after operation: Add soft cooked cereals, custards, soft mashed potatoes and pureed vegetables, soft boiled or poached eggs, gelatine desserts, etc. *Do not force children to eat but be sure they take ample fluids.* Ordinary chewing between meals is helpful in relieving pain from throat spasm.

3rd day after operation: Cooked meat, if finely cut up and properly chewed, may be added to the diet. In the next four days the diet should gradually return to normal except that *dry toast, crackers and other similar foods should be avoided.*

Highly seasoned and hot foods or drinks, and all alcoholic beverages, must be avoided for a period of two weeks following operation. Beer may be taken in small quantities after one week.

6. Moderate pain in the ears and slight fever (up to 100° F.) are common and of no significance. A hot water bottle or heating pad applied over the ears usually affords relief. If severe, constant, throbbing pain should develop in the ear, accompanied by fever of over 100° F., notify me or call your physician.

7. If any bleeding occurs, the patient should sit erect and gargle with a mixture of 1 part of hydrogen peroxide solution and 3 parts cool water. Ice may also be sucked. If these measures do not control the bleeding, notify me, or take the patient back to the hospital in a car without delay.

8. The patient should return to my office on at for examination of the throat and further instructions.

In spite of these measures, which are almost universally stressed, the incidence of late tonsillar bleeding is generally acknowledged to be approximately 10 per cent.[1-5] (In the author's control series the incidence was 9.9 per cent.) In 1945, Singer[6] pointed out that in Austria, where he formerly practiced, late tonsillar bleeding seemed much less common. In his experience the only significant difference in the management of the cases on the two continents is the widespread use of aspirin here, whereas aminopyrine is the analgesic of choice in Central Europe. Neivert[1] pursued Singer's observations and postulated that the high incidence of late bleeding observed in this country was probably due to a salicylate-induced prothrombinemia. He attempted to prove that the administration of vitamin K would reduce the incidence of late tonsillar bleeding by preventing such a prothrombinemia. In a series of 283 patients who were given vitamin K along with aspirin following tonsillectomy, he reported a decrease in late hemorrhage from his previous 10 per cent incidence to an incidence of 1.4 per cent.

The author began his studies of late tonsillar bleeding immediately after the publication of Neivert's work but was not able to duplicate Neivert's results.[3] In subsequent published reports it developed that Neivert was administering

moderately large doses of aspirin orally, whereas the author primarily used aspirin in the form of chewing gum. This might account for some differences in prothrombin blood levels in the patients in the two series.

It is conceded that very large doses of salicylate may reduce the prothrombin level of the blood, and that vitamin K will protect such an individual from such a prothrombin depletion if administered along with the salicylate. Quick,[9] however, emphasizes that prothrombinemia becomes clinically significant only if the prothrombin falls below 20 per cent of normal, as it is not until then that the patient is in danger of hemorrhage.

It is the author's opinion that most otolaryngologists do not employ aspirin in such large doses after tonsillectomy, but that the vast majority of aspirin prescribed is in the form of aspirin chewing gum. It was difficult to conceive that the relatively moderate doses of salicylate ingested during the usual postoperative period could deplete the prothrombin to such an extent as to place otherwise normal patients in danger of hemorrhage.

Since the administration of vitamin K along with the indiscriminate use of aspirin chewing gum had no effect whatever on the incidence of late tonsillar bleeding in the author's series, it was felt there must be other causes for such bleeding, and efforts were directed toward establishing possible adverse local effects of such aspirin.[3]

Livingston and Neary[7] subsequently reported a small series of 45 tonsillectomies in which prothrombin studies were made. Twenty-nine of this group received five to six tablets of aspirin chewing gum daily (approximately 20 gr. daily) from the first to the seventh postoperative day. There was an incidence of 6.6 per cent of late tonsillar bleeding, and there was no decrease of blood prothrombin in any of the cases. A control group of 16 patients received aspirin chewing gum in similar dosage and, in addition, 0.5 mgm. of synthetic vitamin K. The incidence of late tonsillar bleeding was 6.3 per cent, and again no change in blood prothrombin was noted. They

concluded that . . . "there is no indication that the routine post-tonsillectomy use of chewing gum containing acetylsalicylic acid may give rise to prothrombinopenic hemorrhage or that such use of this gum has any adverse effect on blood prothrombin." We were able to confirm this in three cases of late bleeding in patients who had used aspirin chewing gum indiscriminately and who had taken no vitamin K or any other medication. Prothrombin blood levels were determined at the time of the bleeding, and all were found to be well within normal limits.

Preston[2] reported that in a series extending over a five-year period, secondary tonsillar hemorrhage occurred in from 4.29 to 7.07 per cent of the patients who used aspirin alone; and that in 385 patients to whom he gave vitamin K simultaneously with aspirin, the incidence of late tonsillar bleeding was reduced to 2.08 per cent. It is not entirely clear how much aspirin was given and exactly in what form.

None of the above workers described the exact method employed to determine the percentage of late tonsillar bleeding, other than their observations in the office or clinic approximately one week after surgery. This point of possible error is stressed since, in our experience, using detailed questionnaires with careful and persistent follow-up by mail and phone, the percentages finally determined showed marked discrepancies with the original figures obtained from our case records alone. Our studies were made entirely with the use of such questionnaires (see Fig. 2), and cases in which such follow-up studies were not possible were omitted from the series.

After studying 246 cases of tonsillectomy, Jones[10] concludes that "acetylsalicylic acid should not be prescribed for ingestion in sufficient quantities to cause hypoprothrombinemia; and should not be prescribed, in any form, for local administration following tonsillectomy." He also feels that "adequate vitamins C and K should be prescribed preoperatively and postoperatively to maintain a high prothrombin concentration," and that efforts should be directed at preventing postoperative infection of the operative sites.

FIGURE 2.

DR. SAMUEL L. FOX
1205, St. Paul St., Baltimore 2, Md.

RE: John Doe

Dear Mrs. Doe:

I am making a survey of all the patients operated upon by me for tonsillectomy and adenoidectomy. I would greatly appreciate your answers to the following questions. An addressed, stamped envelope is enclosed for the return of this questionnaire.

Thanking you for your courtesy, I am

Very truly yours,

(Signed) SAMUEL L. FOX, M.D.

PLEASE FILL IN THE BLANKS

1. Did any bleeding occur after leaving the hospital?.....

2. If so, when did it occur?.....

Was medical attention required?.....

Please describe .....

.....

3. Was any lozenge or other medication used?.....Please describe

.....

Did it help? .....

4. Was any Aspergum chewed after operation?.....

If so, how many boxes were used?.....

PLEASE RETURN THIS QUESTIONNAIRE IN THE ENCLOSED ENVELOPE

Considering the possible local effect of aspirin upon the wound further, it was found that Ersner *et al.*[8] had previously shown that when saliva and blood are mixed, the blood coagulation time is shortened. A mixture of saliva, blood and aspirin solution, however, showed a definite interference with blood coagulation, and other such strongly acid solutions produced similar effects. When aspirin is dissolved in saliva (or other aqueous menstrua) hydrolysis of the compound is quickly effected and free salicylic acid is liberated. The author feels that such free acid affects the integrity of the coagulum, digesting and loosening it prematurely. The exposed granulating surface is further subjected by the acid-containing saliva to a prolongation of the coagulation time of its exposed and bleeding capillaries. Hemorrhage is thus induced and sustained.

OUR SERIES.

In an effort to determine what factors are most important in the production (and avoidance) of late tonsillar bleeding, an extensive study was undertaken, in which the aggregate number of cases studied now totals 1,746. All cases were operated upon by the same method (sharp dissection of the tonsils, and the use of curettes for the adenoids), and the postoperative management was guided by the same set of printed instructions (see Fig. 1). The only variations were those instituted for each group, as indicated below, to study a particular problem of the cause of late tonsillar bleeding.

Group I consisted of 252 patients who were permitted to use aspirin chewing gum as desired. No other medication was prescribed, except codeine for the adults. This constituted the *control group*. There were 25 cases of late bleeding, an incidence of 9.9 per cent. In three of these cases it was possible to have prothrombin determinations made at the time of bleeding. The results were normal in all three cases.

Group II consisted of 128 patients who were divided into two subgroups. Seventy-eight of these patients were per-

mitted to use aspirin chewing gum as desired, but also took 20 mgm. of synthetic vitamin K daily for seven days postoperatively to counteract any prothrombinemia that might have resulted. No other medication was prescribed, except codeine for the adults. There were eight instances of late bleeding in this group, an incidence of 10.2 per cent. The remaining 50 patients were also permitted to use aspirin chewing gum as desired, but they were given 200 mgm. of ascorbic acid (vitamin C) daily in addition to the 20 mgm. of synthetic vitamin K. There were five instances of late bleeding in this group, an incidence of 10 per cent. Prothrombinemia was obviously not the answer to the problem.

Group III consisted of 576 patients who did not use aspirin chewing gum at all. No vitamin K or vitamin C was given, but codeine was prescribed for the adults. No other medication was prescribed or forbidden. There were eight cases of late bleeding in this group, an incidence of 1.3 per cent. This confirmed our belief that the principal cause of secondary bleeding is due to local and not to constitutional effects.

Group IV consisted of 202 patients who did not use aspirin chewing gum. No vitamin K or vitamin C was taken, but codeine was prescribed for the adults. In addition, they were encouraged to use a lozenge containing tyrothricin and a local anesthetic agent* during the postoperative period. There were two cases of late bleeding, an incidence of 0.99 per cent.

Group V consisted of 419 patients who did not use aspirin chewing gum. No vitamin K or vitamin C was taken, but codeine was prescribed for the adults. In addition, all patients were given an intramuscular injection of 300,000 units of procaine-penicillin immediately postoperatively (during the reaction period) and on the morning following operation. There were four instances of late bleeding in this group, an incidence of 0.95 per cent.

Group VI consisted of 167 patients who were managed exactly as those in Group V with the exception that they used a

tyrothricin-anesthetic lozenge* freely during the postoperative period. There were three cases of late bleeding, an incidence of 1.8 per cent.

At present, studies are being conducted on the effect of sulfathiazole gum on post-tonsillectomy bleeding.* The use of penicillin and aureomycin in lozenge or chewing gum form has been tried but abandoned because of the large number of local reactions, many of which were very severe.

TABLE 1. SECONDARY BLEEDING AFTER TONSILLECTOMY.

Group	Conditions of Series	Total Cases	No. Cases Bleeding	Percentage Bleeding
Group I	Control group Aspergum *ad lib.* No vitamin K or C	252	25	9.9
Group II	*a.* Aspergum *ad lib.* Vitamin K	78	8	10.2
	b. Aspergum *ad lib.* Vitamin K Vitamin C	50	5	10.0
Group III	No aspergum No vitamin K or C	576	8	1.3
Group IV	No aspergum No vitamin K or C Tyrothricin lozenges *ad lib.*	202	2	0.99
Group V	No aspergum No vitamin K or C Penicillin-procaine i.m.	419	4	0.95
Group VI	No aspergum No vitamin K or C Penicillin-procaine i.m. Tyrothricin lozenges *ad lib.*	167	3	1.8

SUMMARY AND CONCLUSIONS.

1. A series of 1,746 consecutive cases of tonsillectomy has been studied in an effort to determine the causes and the methods of prevention of postoperative bleeding.

*The author acknowledges credit to Sharpe and Dohme for supplying "Tyrozets" and to the White Laboratories for supplying "Lozilles" and "Sulfathiazol Gum" for this study. Both of these tyrothricin preparations had a high patient-acceptance rating. "Amotrocin" was also supplied by McNeill Laboratories but was not so acceptable to the patients.

2. Bleeding following tonsillectomy and adenoidectomy may be classified into primary and secondary types. The causes and management of primary bleeding and of secondary bleeding are different and unrelated.

3. Primary bleeding is almost always due to faulty surgical technique or to some constitutional disorder which interferes with the proper clotting of blood. Secondary (late) bleeding results largely from secondary infection of the wound, local trauma to the operative site or from the effects of certain drugs, notably aspirin.

4. The simultaneous administration of vitamin K (with or without vitamin C) while using aspirin chewing gum effected no decrease in the incidence of secondary hemorrhage in this series, whereas the elimination of the use of aspirin chewing gum during the postoperative period caused the incidence of late tonsillar bleeding to be reduced from 9.9 to 1.3 per cent.

5. Whereas it is conceded that very large doses of aspirin or other salicylates may reduce the prothrombin level of the blood, and that the simultaneous administration of vitamin K will protect against such a prothrombin depletion, it is felt that most otolaryngologists do not employ aspirin in such large doses after tonsillectomy but rely rather on the use of aspirin chewing gum. This is thought to exert an adverse local effect upon the coagulum covering the wounds.

6. The use of tyrothricin-anesthetic lozenges postoperatively has had no effect in reducing late tonsillar bleeding but has provided a measure of comfort to the patient and has visibly reduced secondary infection of the operative wounds.

7. The parenteral administration of long-acting procaine-penicillin has produced a possible further slight reduction in the incidence of late tonsillar bleeding (0.95 per cent) and has reduced postoperative sequela and complications.

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TREATMENT OF HYPERPLASTIC SINUSITIS.*†

LOUIS E. SILCOX, M.D.,
Philadelphia, Pa.

The problem of treatment in patients with hyperplastic sinusitis has proven to be a real challenge from the earliest rhinologist down to the present day specialist. The various theories of etiology and causative agents are legion and the story is replete with failures to cure or alleviate the symptoms of this annoying ailment. Numerous scientific treatises have been written extolling the virtues of therapeutic skills ranging from injections of dust extracts to radical sinus surgery without taking full cognizance of one of the fundamental factors in the pathogenesis of this common disease process, namely, bacterial hypersensitivity. It is generally known that there are two schools of thought on the etiology of hyperplastic sinusitis and both groups have their outstanding proponents. One school believes that the nonbacterial allergens are the primary factors and that infection is a secondary development. The other maintains that the hyperplastic changes are due to a primary bacterial infection which acts as the allergenic agent. My observations support the latter view.

Most authorities agree that between 70 and 80 per cent of all cases of chronic sinusitis have allergy as their basic pathology and without adequate attention to this important factor the treatment in these cases is destined to failure. The atopic or nonbacterial allergies have been carefully and thoroughly studied in reference to the sinus tract by Hansel[1] and others. but there is a paucity of fundamental clinical data on bacterial hypersensitivity and the important part it plays in the pathogenesis of chronic hyperplastic sinusitis.[2]

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Goodale,[3] as early as 1916, observed sensitivity to bacteria in the sinus tract and regarded it as an allergic manifestation. He felt that an allergic individual who shows negative skin tests is sensitive to bacteria.

It is common knowledge that allergy to bacterial protein does occur, and this phenomenon is connected with many diseases such as streptococcal infections, rheumatic fever, undulant fever, typhoid fever, and others, but is best known in tuberculosis because of the discovery of the allergic reaction in the skin of those infected by tubercle bacillus.

Zinsser[4] has stated that in allergy to bacterial infection the body is sensitized by antigenic substances which are absorbed from any focus in which bacteria react with inflammatory tissues and as a result the body is rendered sensitive to contact with these same autolytic products whether they are absorbed from a chronically existing focus or from an identical infection subsequently acquired.

There are many physicians who do not accept hypersensitivity to infecting bacteria as an explanation of pathologic changes such as hyperplastic sinusitis because the skin reactions obtained with bacterial products frequently are of a delayed and inflammatory nature instead of the immediate urticarial type obtained with simple protein extracts. There are others who believe that a patient with focal infections in his teeth, tonsils, sinuses or prostate acquires a sensitivity to the bacterial protein which is similar to that of nonbacterial allergens and that these infecting bacteria and their products alone may cause allergic inflammatory reactions. This type of allergic response repeated at frequent intervals can produce hyperplastic sinusitis, particularly if the micro-organisms are embedded in the membranes of the sinuses. Kistler has demonstrated bacteria in hyperplastic sinus mucosa by microscopic methods as often as by cultural methods, and he found most of the bacteria deep in the tissue near the periosteum becoming fewer toward the epithelial surface.

Grove and Cooke[5] feel that hyperplastic sinusitis is caused solely by infection which produces a special pathologic re-

sponse conditioned by the allergic constitution of the patient. Grove and Farrior[6] found bacteria in 80 per cent of the hyperplastic ethmoid and sphenoid membranes at operation, and 96 per cent of the hyperplastic maxillary sinus membranes showed bacterial growth. Grove states that in his experience almost 100 per cent of the pathologic manifestations of sinusitis are of the hyperplastic or thickened membrane type.

Schenck[7] made the observation that allergic ethmoidal tissue cannot combat infection adequately and chronic infection which favors bacterial sensitivity results.

In hyperplastic sinusitis the stroma may contain an abundance of migratory cells: polymorphonuclears, lymphocytes and plasma cells, and with allergy as a prominent factor a varying percentage of eosinophiles will be present. The cellular elements are usually situated around the veins and lymphatics, producing a periphlebitis and perilymphangitis. These inflammatory processes result in obstruction of these respective vessels, causing a loss of fluid into the tissues, which distends the stroma of the tunica propria. This, in turn, is followed by various degenerative changes in the surface epithelium and glands with distension of the tissues and polyp formation.

A chronic inflammatory process in the sinuses will show an increased number of eosinophiles, but Eggston[8] states that their presence does not necessarily indicate allergy in the ordinary sense of the word; he feels that if the term is broadened to include bacterial allergy it may prove the argument that their presence means allergy.

Bacterial allergy should be looked upon as an increased alertness of the body cells toward bacilli and bacillary protein developed as a part of specific resistance, but only necessary until such time as immunity can be established. Following bacterial invasion the body seeks to protect itself against bacterial substances by the production of antibodies. The bacterial substances chemically are cell body proteins including endo- and exotoxins, other nitrogenous products, and carbohydrates. The immune bodies include agglutinins, antitoxins,

precipitins, and in response to bacterial protein substances, there are created important antibodies concerned with bacterial allergy of the tuberculin type. The general idea seems to be that allergy is a phase in the direction of immunity and the greater the sensitivity the higher the immunity.

Kolmer[9] states that allergy to bacteria or their products is important in the mechanism of infection and immunity.

Certainly the trend today in practitioners and specialists alike is to ignore the rôle of immunity in the resistance of the individual to respiratory infections and treat each attack of major or minor severity with chemotherapy or antibiotics. This not only deprives the patient of nature's most potent weapon to combat infection, but also exposes many of the allergic individuals to antibiotic sensitivity, occasionally making the treatment worse than the disease.

The immunity produced by a moderately severe respiratory infection may last from a few weeks to several months and give protection against other similar bacterial infections for varying periods of time, depending upon the type and virulence of the organisms.

Because of the tendency of the medical profession to treat so many respiratory infections with antibiotics, it seems pertinent to emphasize again the value and virtues of stimulating the patient's own defenses by means of autogenous vaccines.

The patients in this study comprise a group with allergic backgrounds or family histories of allergy and are either not skin sensitive to the ordinary allergens — inhalants, foods and pollen, or whose symptoms of recurring sinusitis are not alleviated by controlling these offending substances. These are patients in whom primary bacterial infection causes mucosal changes in the sinuses. The reaction to the bacterial protein is an allergic one because of the constitutional tendency of the patient. The respiratory mucosa of the upper and lower tracts have much in common, and it is logical to assume that if asthmatic attacks can be controlled by reducing allergic responses in the pulmonary tract with vaccine therapy,

then many of the allergic reactions in the sinus mucosa might be reduced to a minimum if the proper organisms could be obtained for antigenic activity. If these allergic edema reactions can be controlled or minimized by this method, the fundamental pathology of most chronic sinusitis could be checked. This study was made in an effort to substantiate this thesis.

The complete study of each patient included rhinoscopy, nasopharyngoscopic examination, allergy skin tests, sinus X-rays, and bacteriologic cultures.

In this presentation there are 200 patients with respiratory allergy, of whom 133 had hyperplastic mucosal changes in one or more sinuses without evidence of pus formation and 67 who had gross purulent secretion in at least one sinus, in addition to the hyperplastic changes. There were 121 adults and 79 children in this series.

Bacteria for vaccine preparation for the 200 patients were obtained from the following sources:

Middle meatus	144
Sinus mucosa at operation	21
Maxillary sinus irrigation	10
Nasopharynx	9
Adenoids at operation	8
Bronchoscopic aspiration	8

The incidence of bacteria cultured for use in vaccines is as follows:

Hemolytic staphylococcus aureus	92
Streptococcus viridans	78
Pneumococcus	75
Hemolytic streptococcus	66
Nonhemolytic staphylococcus aureus	29
Nonhemolytic streptococcus	31
Nonhemolytic staphylococus aureus	29
Hemolytic staphylococcus albus	23
Neisseria catarrhalis	19
Diphtheroids	3
K. pneumoniae	1
Proteus	1
Total	459

In discussing the bacteriology of the nose and sinuses, Eggston[8] and Wolff state that normally these structures contain very few bacteria, and their observations indicate that the most important organisms from the pathologic standpoint are the hemolytic streptococci, hemolytic staphylococcus aureus, anaerobic streptococci and pneumococci.

Castellani, in 1905, showed that when two organisms were injected into an animal simultaneously the antibody response to each organism was equal to that produced by injection of the individual organisms. A good general principle to follow in the preparation of mixed autogenous vaccines is that they should contain as few different bacteria as possible and should include only those which are known or suspected to be pathogenic.

There were 30 patients in this series who had a pure culture of one organism. The bacteria found in pure culture were in this order of frequency:

Hemolytic staphylococcus aureus	12
Beta hemolytic streptococcus	8
Hemolytic staphylococcus albus	6
Streptococcus viridans	2
Pneumococcus	1
Nonhemolytic staphylococcus aureus	1

Two different organisms were cultured and included in vaccines for 89 patients; three organisms in 65; four organisms in 14, and five different bacteria were incorporated in the vaccines of two patients.

The question has been asked many times concerning these patients as to the advisability of using a stock vaccine, inasmuch as they have a wider spectrum of bacterial proteins and are much easier to obtain. That question is answered by stating that one must rely upon clinical experience rather than laboratory observations in determining which type of vaccine to use. Since antigenic qualities do not remain unchanged by artificial cultivation as evidenced by loss of capsules, dimunition of virulence, etc., it is highly advisable that the organisms causing the infection be obtained and included in the vaccine

as quickly as possible. The existence of serologically specific types of bacteria is well known, and it would require a mixture of from 50 to 60 different strains of various bacteria in a stock vaccine if protection against all the serologic types was desired. The use of a properly prepared autogenous vaccine reduces to a minimum the risk of using a different strain and this ability to utilize freshly isolated strains of virulent bacteria unchanged by prolonged cultivation is the main advantage of an autogenous vaccine in addition to the fact that freshly prepared vaccines are more antigenic than old stock ones.

The vaccines in this study were prepared by two different methods: 110 were prepared by the heat killed method in which the bacteria were rendered nonviable by submerging the bottles containing the filtered suspension of bacteria in a water bath at 60° C. for one hour on two successive days; 90 vaccines were prepared by the chemically killed method in which phenol or tricresol is used to inactivate the mixture of bacteria.

From each vaccine a dilution of 100,000,000 killed organisms per cubic centimeter and another of 2,000,000,000 per cubic centimeter was made by use of the McFarland nepholometer tubes for comparison. Sterility tests were done on all vaccines.

Intradermal tests were done routinely with 0.05 cc. of the weaker dilution of the vaccine. Immediate or delayed positive skin reactions were obtained in 36.3 per cent of the 110 patients who were tested with heat killed vaccines and 77.5 per cent of the 90 patients who were tested with the chemically killed vaccines. There are divergent views on the reliability of skin tests with bacterial extracts, and most observers disregard them from a diagnostic standpoint. I do the testing routinely to be certain that the vaccine is not too strong for the patient, and in 10 per cent of the chemically killed vaccines I found it necessary to dilute the vaccine from 100,000,000 to 10,000,000 killed organisms per cubic centimeter to prevent local and general reactions. The reactions from chemi-

cally prepared vaccines are probably due to the toxins which are preserved by this method. Benson[10] states that the reactions of intradermal tests in conjunction with the systemic effects of bacterial inoculation form the most reliable guide to vaccine therapy in cases of bacterial hypersensitivity of the respiratory tract.

Successful vaccine therapy in hyperplastic sinusitis requires proper administration, which implies giving the optimum dose to the patient at the optimum interval. The optimum dose of vaccine is the amount which produces a favorable reaction, an improvement in the symptoms and maintains the longest interval of improvement. Each subsequent dose is regulated according to the general or local reactions produced by the preceding dose. It is my custom to start with 0.05 cc. of the weaker dilution and increase the dose by that amount at five-day intervals, which is the period of time that the favorable effect of the preceding dose is just beginning to wear off. If reactions occur, and they commonly do with chemically killed vaccines being observed in over 50 per cent of this series, then the same dose is repeated, and if the reaction is severe the dose is reduced. Rackemann and Graham showed that successful results with bacterial vaccines were dependent upon the production of definite local reactions to the therapeutic doses and that results were not obtained with vaccines which failed to produce these local reactions. Autogenous vaccines are as individual as one's personality and treatment with them must be empirical. When the patient has received 1 cc. of the weaker dilution, the stronger concentration of 2,000,000,000 organisms per cubic centimeter is given in a similar manner, starting with 0.05 cc. and increasing until 1 cc. is reached.

Autogenous vaccine therapy rests on an inadequate basis of experimental evidence but has definitely taken a place among other empirical remedies with a certain amount of specificity in hyperplastic sinusitis. Grove reported that 75 per cent of a group who had antrum window resections showed mucous membrane sensitivity to their vaccines and often a specificity to one organism when several were recov-

ered. Not only could asthma be produced but also marked edematous swelling of the lining membrane, almost obliterating the sinus, and an outpouring of mucus loaded with eosinophiles.

Autogenous vaccine therapy in hyperplastic sinusitis is not infrequently doomed to defeat from the outset by failure to incorporate organisms of primary infection because of faulty bacteriologic methods, as well as improper preparation and careless methods of administration.

Advocates of autogenous vaccine therapy do not intend to neglect other rational forms of treatment. Conditions demanding surgical intervention such as irreversible sinus pathology, suppurative foci and obstructing polyps should be treated surgically and all primary foci of infection should be eradicated or drained.

From the complete study of each patient and his response to vaccine therapy a clinical impression was made as to whether his sinus pathology was reversible or irreversible. One hundred twenty-eight, or 64 per cent, had hyperplastic changes which were considered to be reversible and 72, or 36 per cent, were thought to have irreversible changes in one or more sinus. Of the 72 patients with irreversible changes, only 21 would permit the sinus surgery that was indicated, and the remaining 51 preferred not to have their focal infection removed because of advice received from family physicians or friends who warned against any nasal surgery on the grounds that the patients' symptoms would be made worse. This is a common belief among the profession and laity alike and probably founded on the poor results obtained from nasal and sinus surgery prior to the recognition and control of allergy in the pre- and postoperative periods. It has been my policy to administer autogenous vaccines and maintain the patient on a strict allergic regime before and after sinus surgery in the hope that the patient's increased antibody response and his decreased allergic reaction to bacterial protein will help protect the new sinus membrane from hyperplastic changes.

Of the 21 patients who consented to surgery, 14 had bilateral Caldwell-Luc operations, four had antral window resec-

tions, two had bilateral ethmoidectomies, and one patient had a radical frontal sinus operation of the Killian type. All of these patients had excellent clinical results except two of the cases with antral window resections in which diseased hyperplastic membrane remained in the sinuses.

Of the 51 patients with irreversible pathology in the sinuses who refused sinus surgery, 37 were clinically improved with autogenous vaccine therapy as long as they received injections at regular intervals. Many of this group were careless about the regularity of their injections and some who missed three or four injections had exacerbations of their symptoms; with a lapse of several months six patients had as much trouble as they did prior to any treatment. These observations indicate the importance of eliminating focal infection and the necessity of prolonged regular injections if satisfactory results are desired with autogenous vaccine therapy.

Of the 128 patients whose sinus pathology was thought to be reversible, 114 were either improved or markedly improved, 10 were unchanged and four were made worse by their autogenous vaccines.

SUMMARY.

A group of 200 allergic patients with hyperplastic sinusitis who were treated with autogenous vaccines is presented. One hundred seventy were improved or markedly improved, 26 were not improved and four were made worse by this treatment. They ranged in age from 10 months to 74 years and the average period of treatment was 10 months. Skin tests with the vaccines were positive in 56.9 percent. This study further substantiates the thesis that bacterial hypersensitivity is an important factor in the pathogenesis of hyperplastic sinusitis and that autogenous vaccine therapy is a potent agent in the treatment of this disease.

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AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY HOME STUDY COURSES.

The 1952-1953 Home Study Courses in the basic sciences related to opththalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on Sept. 1, 1952, and continue for a period of 10 months. Detailed information and application forms can be secured from Dr. William L. Benedict, executive secretary-treasurer of the Academy, 100 First Avenue Building, Rochester, Minn. Registrations should be completed before Aug. 15.

1952 SUMMER MEETING, VOLTA SPEECH ASSOCIATION FOR THE DEAF.

The 1952 Summer meeting of the Volta Speech Association for the Deaf will be held in New England, June 16-20, 1952. Theme: "That the Deaf May Speak."

The program will begin on June 16 in Northampton, Mass., when the Clarke School will welcome our Association members with a series of demonstrations. The Clarke program will end Tuesday at noon and the opening session of the main convention will be held Tuesday evening, June 17, at the Hotel Kenmore, 490 Commonwealth Avenue, Boston, at 8 p.m.

The program will continue Wednesday, Thursday and Friday at the Horace Mann School and the Hotel Kenmore.

Members may register either in Northampton, Mass., or Boston.

NATHAN P. HARRIS, Program Chairman.

In Memoriam

LOUIS K. GUGGENHEIM, M.D.,

1884-1952.

Dr. Louis K. Guggenheim died suddenly on March 13, 1952, in his home in Westwood Village, Los Angeles, Calif., from dissecting aneurysm of the thoracic aorta with rupturing into the pericardial sac. He was 68 years old.

Dr. Guggenheim was born in Cincinnati, Ohio, March 3, 1884. He received his medical degree cum laude from Washington University in St. Louis, Mo., in 1905. After doing postgraduate work at St. Louis City Hospital, Dr. Guggenheim went to Vienna where he served as a senior interne from 1906 to 1908, and to Berlin where he served in the same capacity from 1908 to 1909. He frequently returned to Europe for further study in the field of otolaryngology. He practiced in St. Louis from 1909 to 1936, when he moved to Los Angeles. He continued the practice of otolaryngology in Los Angeles until 1950 when he entered the field of psychoanalysis, which he was practicing at the time of his death. Dr. Guggenheim held the following positions: Associate Professor of Otolaryngology, University of Southern California; formerly Assistant Professor of Otolaryngology, Washington

University School of Medicine; formerly Research Associate, University of California at Los Angeles.

He was a member of Phi Beta Pi National Medical Fraternity, Mu Chapter, Washington University; Fellow of the American Medical Association, the American College of Surgeons, the American Otological Society, the American Laryngological, Rhinological and Otological Society, the American Academy of Ophthalmology and Otolaryngology, etc. He was a former staff consultant of St. John's Hospital, Santa Monica, Calif., and a former staff member of the Los Angeles County General Hospital, the Los Angeles Eye and Ear Hospital and the Children's Hospital of Los Angeles, where he conducted a hearing clinic from 1937 to 1942 in connection with an almost lifelong research project.

Dr. Guggenheim was the author of three scientific books: "Otosclerosis," "Phylogenesis of the Ear" and its logical sequel, "The Embryology of the Human Ear," which is currently being edited for posthumous publication. He presented his book "Phylogenesis of the Ear" to all the universities of the world. He was also the author of many original articles in his specialty.

He leaves his widow, Mrs. Eleanor Anita Guggenheim, a daughter, Mrs. Mary Ewalt, and a son, Dr. Paul Guggenheim, of Council Bluffs, Iowa.

HEARING AIDS ACCEPTED BY THE COUNCIL ON PHYSICAL MEDICINE OF THE AMERICAN MEDICAL ASSOCIATION.

April 1, 1952.

Audicon Models 400 and 415.
Manufacturer: National Earphone Co., Inc., 20-22 Shipman St., Newark 2, N. J.

Audivox Model Super 67.
Manufacturer: Audivox, Inc., 259 W. 14th St., New York 11, N. Y.

Aurex Models L and M.
Manufacturer: Aurex Corp., 1117 N. Franklin St., Chcago, Ill.

Beltone Symphonette; Beltone Mono-Pac Model M.
Manufacturer: Beltone Hearing Aid Co., 1450 W. 19th St., Chicago, Ill.

Cleartone Model 500; Model 700; Cleartone Regency Model.
Manufacturer: American Sound Products, Inc., 2454 S. Michigan Ave., Chicago 16, Ill.

Dahlberg Model D-1; Dahlberg Junior Model D-2.
Manufacturer: The Dahlberg Co., 2730 W. Lake St., Chicago 16, Ill.

Dysonic Model 1.
Manufacturer: Dynamic Hearing Aids, 43 Exchange Pl., New York 5, N. Y.

Electroear Model C.
Manufacturer: American Earphone Co., Inc., 10 East 43rd St., New York 17, N. Y.

Gem Hearing Aid Model V-35; Gem Model V-60.
Manufacturer: Gem Ear Phone Co., Inc., 50 W. 29th St., New York 1, N. Y.

Maico Atomeer; Maico UE-Atomeer; Maico Quiet Ear Models G and H; Maico Model J.
Manufacturer: Maico Co., Inc., 21 North Third St., Minneapolis 1, Minn.

Mears (Crystal and Magnetic) Aurophone Model 200; 1947—Mears Aurophone Model 98.

Manufacturer: Mears Radio Hearing Device Corp., 1 W. 34th St., New York, N. Y.

Micronic Model 303; Micronic Model "Mercury"; Micronic Star Model.

Manufacturer: Micronic Co., 727 Atlantic Ave., Boston 11, Mass.

Microtone T5 Audiomatic; Microtone Classic Model T9; Microtone Model T10; Microtone Model T612; Microtone Model 45.

Manufacturer: Microtone Co., Ford Parkway on the Mississippi, St. Paul, Minn.; Minneapolis 9, Minn.

National Cub Model C; National Cub Model D (Duplex); National Standard Model T; National Star Model S; National Ultrathin Model 504; National Vanity Model 506.

Manufacturer: National Hearing Aid Laboratories, 815 S. Hill St., Los Angeles 14, Calif.

Otarion Model E-4; Otarion Models F-1, F-2 and F-3; Otarion Model G-2.

Manufacturer: Otarion Hearing Aids, 159 N. Dearborn St., Chicago, Ill.

Paravox Model D, "Top-Twin-Tone"; Model J (Tiny-Mite); Paravox Model XT (Xtra-Thin); Paravox Model XTS (Xtra-Thin); Paravox Model Y (YM, YC and YC-7) (Veri-Small).

Manufacturer: Paravox, Inc., 2056 E. 4th St., Cleveland, Ohio.

Radioear Permo-Magnetic Multipower; Radioear Permo-Magnetic Uniphone; Radio Ear All Magnetic Model 55; Radioear Model 62 Starlet; Model 72.

Manufacturer: E. A. Myers & Sons, 306 Beverly Rd., Mt. Lebanon, Pittsburgh, Pa.

Rochester Model R-1; Rochester Model R-2.

Manufacturer: Rochester Acoustical Laboratories, Inc., 117 Fourth St., S.W., Rochester, Minn.

Silvertone Model 103BM.
Manufacturer: National Hearing Aid Laboratories, 815 S. Hill St., Los Angeles 14, Calif.
Distributor: Sears-Roebuck & Co., 925 S. Homan Ave., Chicago 7, Ill.

Silvertone Model J-92.
Manufacturer: Sears-Roebuck Co., 925 S. Homan Ave., Chicago 7, Ill.

Silvertone Model P-15.
Manufacturer: W. E. Johnson Mfg. Co., 708 W. 40th St., Minneapolis, Minn.
Distributor: Sears, Roebuck & Co., 925 S. Homan Ave., Chicago 7, Ill.

Solo-Pak Model 99.
Manufacturer: Solo-Pak Electronics Corp., Linden St., Reading, Mass.

Sonotone Model 700; Sonotone Model 900; Sonotone Models 910 and 920; Sonotone Model 925; Sonotone Model 940; Sonotone Model 966.
Manufacturer: Sonotone Corp., Elmsford, N. Y.

Superfonic Hearing Aid.
Manufacturer: American Sound Products, Inc., 1303 S. Michigan Ave., Chicago 5, Ill.

Televox Model E.
Manufacturer: Televox Mfg. Co., 1307 Sansom St., Philadelphia 7, Pa.

Telex Model 22; Telex Model 97; Telex Model 99; Telex Model 200; Telex Model 300B; Telex Model 400; Telex Model 1700.
Manufacturer: Telex, Inc., Telex Park, Minneapolis 1, Minn.

Tonamic Model 50.
Manufacturer: Tonamic, Inc., 12 Russell St., Everett 49, Mass.

Tonemaster Model Royal; Model Cameo.
Manufacturer: Tonemasters, Inc., 400 S. Washington St., Peoria 2, Ill.

Unex Model "A"; Unex Midget Model 95; Unex Midget Model 110; Unex Models 200 and 230.
Manufacturer: Nichols & Clark, Hathorne, Mass.

Vacolite Models J and J-2.
Manufacturer: Vacolite Co., 3003 N. Henderson St., Dallas 6, Tex.

Western Electric Models 65 and 66.
Manufacturer: Audivox, Inc., successor to Western Electric Hearing Aid Division, 259 W. 14th St., New York 11, N. Y.

Zenith Model 75; Zenith Miniature 75; Zenith Model Royal; Zenith Model Super Royal.
Manufacturer: Zenith Radio Corp., 6001 Dickens Ave., Chicago, Ill.

All of the accepted hearing devices employ vacuum tubes.

Accepted Hearing Aids more than five years old have been omitted from this list for brevity.

TABLE HEARING AIDS.

Aurex (Semi-Portable).
Manufacturer: Aurex Corp., 1117 N. Franklin St., Chicago (10), Ill.

Precision Table Hearing Aid.
Manufacturer: Precision Hearing Aids, 5157 W. Grand Ave., Chicago 39, Ill.

Sonotone Professional Table Set Model 50.
Manufacturer: Sonotone Corp., Elmsford, N. Y.

All of the Accepted hearing devices employ vacuum tubes.

DIRECTORY OF OTOLARYNGOLOGIC SOCIETIES.

AMERICAN OTOLOGICAL SOCIETY.

President: Dr. Gordon D. Hoople, 1100 E. Genesee St., Syracuse, N. Y.
Vice-President: Albert C. Furstenberg, University Hospital, Ann Arbor, Mich.
Secretary: Dr. John R. Lindsay, 950 E. 59th St., Chicago 37, Ill.
Meeting: Royal York Hotel, Toronto, Canada, May 18-19, 1952.

AMERICAN LARYNGOLOGICAL ASSOCIATION.

President: Dr. H. Marshall Taylor, 111 W. Adams St., Jacksonville, Fla.
Secretary: Dr. Louis H. Clerf, 1530 Locust St., Philadelphia 2, Pa.
Meeting: Royal York Hotel, Toronto, Canada, May 23-24, 1952.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

President Dr. C. Stewart Nash, 108 Medical Arts Bldg., Rochester, N. Y.
Meeting: Royal York Hotel, Toronto, Canada (mornings only), May 20-22, 1952.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

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Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis 3, Tenn.

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President: Dr. James M. Robb, Detroit, Mich.
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.
Meeting: Palmer House, Chicago, Ill., Oct. 12-17, 1952.

AMERICAN BOARD OF OTOLARYNGOLOGY.

Meeting: Royal York Hotel, Toronto, Canada, May 13-16, 1952.
Palmer House, Chicago, Ill., October 6-10, 1952.

THE SECTION OF OTOLARYNGOLOGY OF THE MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA.

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Meetings are held on the third Tuesday of October, November, March and May, 7:00 P.M.
Place: Army and Navy Club, Washington, D. C.

AMERICAN COLLEGE OF SURGEONS
SCHEDULE OF SECTIONAL MEETINGS—1952

The Vancouver Hotel, Vancouver, B. C., Monday, Tuesday, Wednesday, March 31, April 1, 2.

The Pioneer Hotel, Tucson, Ariz., Monday, Tuesday, Wednesday, April 7, 8, 9.

Royal York Hotel, Toronto, Canada, Thursday, Friday, Saturday, May 15, 16, 17.

Those who plan to attend a Sectional Meeting may select the meeting which in time or place is most convenient.

THE LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY.

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Vice-President: Dr. W. L. Hughes, Lamar Life Bldg., Jackson, Miss.
Secretary: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

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Meeting: Palmer House, Chicago, Ill., Oct. 11, 1952.

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Meeting: Palmer House, Chicago, Ill., Oct. 17, 1952.

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Executive Secretary: Dr. Chevalier L. Jackson, 1901 Walnut St., Philadelphia 3, Pa., U. S. A.
Meeting: Fourth Pan American Congress of Oto-Rhino-Laryngology and Broncho-Esophagology.
President: Dr. Ricardo Tapia Acuna, Mexico City.
Time and Place: January, 1954, Mexico City.

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Meeting: St. Louis, Hotel Jefferson, Oct. 1-3, 1952.

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Chairman of Eye Section: Dr. Deane Hartman.
Recording Secretary, Eye Section: Dr. Robert Norene.
Time: 6:00 P.M., fourth Monday of each month from September to May, inclusive.

THIRD LATIN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY.

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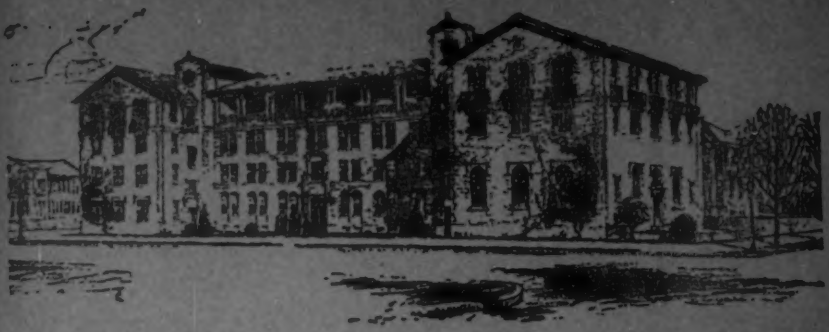

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